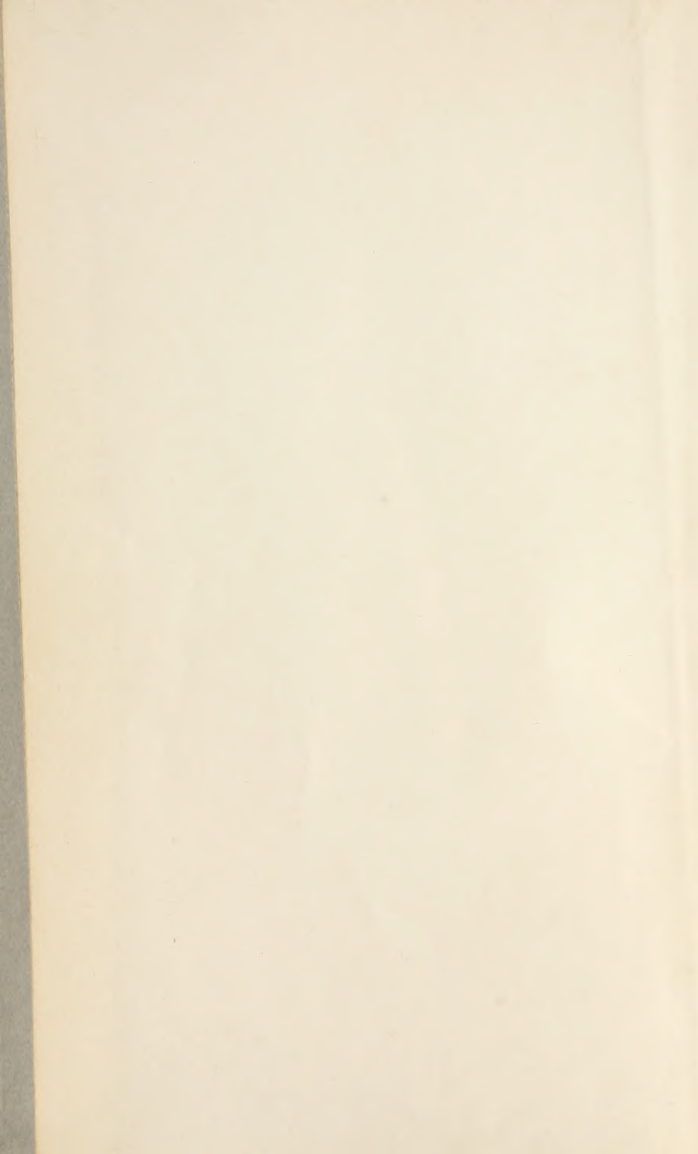


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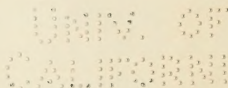
PRACTICAL PATHOLOGY.

A MANUAL FOR STUDENTS AND PRACTITIONERS

BY

mar.
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PREFACE TO THE FOURTH EDITION

My justification for bringing out a new edition of a book that has been out of print for so many years must be that no other work has yet been provided that covers exactly the same ground, and that during the last ten or a dozen years I have received oft-repeated inquiries as to when a new edition might be expected.

Now, more than ever, am I conscious of the impossibility of writing any text-book which will meet the whole needs of the student of Pathology, and I make no pretence that in this work I have achieved the impossible. I might, of course, select a title more intensive than "Practical Pathology" as a descriptive term, but the work has been so long before the public in its present guise that I prefer to send it out as it is, even though it be but a duckling masquerading as a swan.

I have found that, in its present form, "Practical Pathology" is helpful to the medical student in his class work, enables him to continue his practical morbid histology in the ward and in the side-room, and, when he has entered upon his career as a medical practitioner, provides him with readily accessible methods and information that it may be difficult to sift out from the contents of more voluminous tomes. At one time I was tempted to depart from my original plan and to deal more comprehensively with the practical pathology of to-day, so different a thing from that of a quarter of a century ago when the First Edition appeared. The more I considered the question, however, the more satisfied I became that the book was

valuable only because of its distinctive qualities, and that any time or energy I was able to devote to its revision would be best expended in correcting and re-writing it in its original form.

The chapter on Methods has been brought up to date. Only the most useful methods, those of which we have had experience in our Laboratory work, have been included. The chapter on Inflammation and Healing of Wounds has been re-written, and much matter, especially as regards the naked-eye appearances of Diseased Organs, has been added. Class specimens have, in most instances, been taken as the material from which drawings (the number of which has been greatly increased) have been made. Here and there drawings of rare and special specimens have been introduced in order that the student may have some idea of the appearance of some of the objects for which he has to search, but I have tried, throughout, as in former editions, to make the work of our class in Morbid Histology the basis of the book.

To Drs. Alexander Bruce, H. Alexis Thomson, John Thomson, the late D. G. F. Croke, and to Messrs. Macmillan & Co., Mr. Richard Muir (Edinburgh), Dr. Anna Williams (Minneapolis), Dr. James Miller, Dr. James W. Dawson, Dr. Henry Beckton, and my assistants, Mr. E. E. Stubbings and Mr. W. A. Mitchell, I am indebted for most of these special specimens, and to some of them for useful practical hints during the course of the production of this work. To the skill of Mr. R. Muir, Drs. Arthur Clarkson, G. Lovell Gulland, G. A. Fothergill, Mr. J. T. Murray, the late Dr. W. A. Scott, and of my assistant, Mr. H. Gillings, I owe the beautiful drawings from which Messrs. Morrison & Gibb have prepared such satisfactory illustrations. I must also thank Messrs. Macmillan & Co. for permitting me to use the figures in Foster's "Physiology" from which Fig. 203 was prepared. Finally, my hearty thanks are due, and given, to those friends mentioned in the First Edition; to Dr. G. C. Cathcart, to whom I owed so much for his painstaking reading of the Third Edition; to Dr. T.

Watts Eden, for the care and labour he has expended on the revision of the chapter originally contributed by the late Dr. J. Milne Chapman ; to Mr. A. E. Shipley for several suggestive notes relating to the chapter on Animal Parasites ; to my secretary and friend, Mr. F. G. Binnie, for the valuable help he has given to me in the reading of proofs and the preparation of a very full and accurate Index ; and to Mr. Keogh Murphy and the Publishers for the genuine interest they have taken in the preparation of a book by no means easy of production.

G. S. W.

CAMBRIDGE, *January* 10, 1910.

PREFACE TO THE FIRST EDITION

WHILST there are, in abundance, systematic treatises upon Pathology, and the results of researches of those most eminent in the Pathological world are within the reach of all, there is yet a want of a guide to the practical work involved in the study, preparation, and examination of Morbid Tissues. This want, so great as to have become almost a reproach to Pathologists, the author of this handbook has endeavoured to supply. Though vast strides have recently been made in this branch of medical study, one of the most important bases of Clinical Medicine, the Student and the Practitioner have had very scant opportunity of thoroughly acquainting themselves with the appearance of Diseased Organs and Tissues. Acquaintance with naked-eye and microscopic appearances of diseased structures is necessary for the comprehension and appreciation of recent pathological researches, and can be acquired only by a diligent use of the scalpel and the microscope.

The necessity for such practical work was recognised abroad earlier than in our own country. At the present time practical teaching in Morbid Anatomy and Pathological Histology is more general than was formerly the case in our Medical Schools. The Author hopes that his work will greatly aid both Students and Practitioners in familiarising themselves with the methods and results of pathological inquiry, and that it will prove to be an adequate introduction to Systematic Pathology. It is not designed to displace so much as

to aid and supplement oral instruction in Practical Pathology, and to prepare the Student for the Lecture-room, and for the study of more systematic text-books.

The plan adopted is to follow the tissue from the body to the microscope, to describe the method of making the post-mortem and naked-eye examinations, and of preparing the various structures for microscopic investigation. The more important changes of each organ are indicated, though all the changes which occur could not possibly be considered in the space at command. In all cases the aim has been to describe at least the more important typical lesions. In as many instances as possible, illustrations, which are not mere diagrams, are added. Most of the original Drawings have been made from Sections prepared in the course of the work of the Edinburgh University Practical Pathology Class. They may therefore be accepted as representing as faithfully as possible the appearances which may be recognised by any normally intelligent and dexterous student. The copied Drawings, taken from the best sources, are, as far as possible, acknowledged in the descriptions.

The Author is greatly indebted to numerous writers for many of the facts adduced, but has preferred to acknowledge generally his indebtedness rather than to cumber his work with individual references. He is constrained to mention with gratitude the late Professor Sanders's Course of Pathology, and Professor Hamilton's and Professor Greenfield's Courses of Practical Pathology, on the outlines of which two practical courses the work is based. To Professor Greenfield (who kindly allowed the Author to make what use he thought fit of notes taken of his course of Systematic Lectures), he is indebted for much valuable assistance. The Author has found that Professor Ziegler enunciates views similar to those of Professor Greenfield upon the Pathological Histology of Granular Contracted Kidney and Acute Phthisis. He therefore

feels it incumbent upon him to record that Professor Greenfield's investigations were completed and published in Papers and Lectures before Professor Ziegler's excellent Manual of Pathology appeared, and that the two sections (Kidney and Lung) of the present work were already printed when the corresponding sections in Ziegler's Pathology appeared.

Such descriptions as occur of the Normal Histology of various organs are based mainly on Klein and Noble Smith's admirable work. Only such points are referred to as may prove to be of very great assistance in following pathological changes. Every student is advised to make himself thoroughly acquainted with Normal Histology before commencing the study of Morbid Tissues.

In the section dealing with Parasites, the general plan has been departed from in some measure. A few comparatively full descriptions are offered, and in addition merely a list of the more important forms.

As the work was written at intervals between the discharge of more pressing duties, the Author is prepared for many imperfections in it. He thanks most warmly Mr. Robert Robertson, M.B., C.M., and Mr. Mason, for the very full Index which they have compiled; Mr. J. Tatham Thompson, F.R.M.S., for many of the Drawings; Dr. Bendall, and Messrs. W. E. Hoyle, M.A., R. J. Harvey Gibson, M.A., Chas. Kennedy, M.B., C.M., W. B. Mackay, M.B., C.M., and R. Muir for Drawings: Messrs. C. W. Cathcart, F.R.C.S. (*vide* Fig. 127), and W. O. Williams, M.R.C.V.S. (*vide* Figs. 274 and 275), for the loan of preparations from which Drawings have been made.

G. S. W.

EDINBURGH, *October 1, 1883.*

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ERRATA.

- Page 237, line 4 from bottom, *for* "251" *read* "235."
,, 274, ,, 10 from bottom, *for* "266" *read* "273."
,, 307, ,, 6 from bottom, *for* "§§" *read* "§."
,, 768, ,, 3, *for* "particle" *read* "particles."
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PRACTICAL PATHOLOGY

PRACTICAL PATHOLOGY

CHAPTER I

POST-MORTEM EXAMINATION

1. Instruments required—

(a) Two or three “section” knives, strong enough to be used as cartilage knives. The handle must be strong and thick, so that it may be grasped firmly in the palm of the hand; the blade stout, with the belly curved and sharpened up to the commencement of the rounded end (Fig. 1). With these knives, made for me by Mr. Gardner of Edinburgh, there is little or no danger of making punctured post-mortem wounds.

(b) A couple of scalpels, such as are supplied in the ordinary dissecting case.

* (c) For dividing the costal cartilages, Coats’ knife with “a triangular blade, the edge straight, and forming an angle of about 35° with the back, which should be very strong and thick; the handle should be strong, and the blade prolonged through it from end to end,” is recommended.

(d) Two curved bistouries; one probe-pointed, the other sharpened up to the point.

* (e) A hollow-ground razor (Heifor’s army razor), or better, a Valentin’s knife, for cutting thin sections of fresh tissues.

(f) A thin-bladed knife, about 1 inch broad and 10 or 12 inches long, for making complete sections through the various viscera. This is especially useful for opening up the brain, but one rather shorter, though of similar make, may be used for slicing up the other organs. For the first incision into the brain a thin narrow knife, about one-third to one-half inch in breadth, and 10 or 12 inches long, is also exceed-

* Those marked with an asterisk are not absolutely necessary for use in private houses, but they should be included in the equipment of a post-mortem theatre.

ingly useful, but by no means necessary. A curved bistoury and a grooved director are useful.

(*g*) A couple of pairs of dissecting forceps, and a pair of dressing forceps.

* (*h*) Two pairs of double hooks well blunted, with chain; and a couple of copper spatulæ.

(*i*) Two pairs of scissors; "one pair large, having one blade with the point rounded off, the other sharp; the other pair small, one blade probe-pointed, the other sharp-pointed."

(*j*) A pair of intestine scissors, with a long curved and blunt-pointed blade with a hook turned backward, and a shorter square-ended blade which closes behind the hook, so that the curved blade is not cut out of the bowel when the scissors close.

(*k*) A blowpipe, preferably with a stop-cock.

(*l*) Several blunt probes, of different sizes.

(*m*) A small bone-saw, with a strong movable back and fine teeth, well set, and a bone-saw with long curved handle for cutting through the laminæ of the vertebræ.

(*n*) A metal catheter, No. 8, and several flexible catheters.

(*o*) A mallet—or steel hammer with a hook at the end of the handle, which is very useful in laying hold of and lifting the calvaria—and a T-shaped steel chisel; the blade and cross piece of the chisel should each be about 6 inches in length, and the blade, 1 inch broad, may be made with a guard at a distance of about one-third of an inch from the point. This guard is of use when the skull-cap is being removed, but it interferes with the use of the chisel for other purposes, such as cutting out the spinal cord; when the guard is adopted a second straight steel chisel should be added



FIG. 1.

to the list of instruments.

(*p*) One pair of strong bone-forceps, the two ends of the handles of which should be about 2 inches apart when they are forcibly gripped in the hand.

(*q*) Three or four large straight flat "packing" needles, half a dozen curved needles of different sizes, and some strong thin twine.

(*r*) A pair of caliper-compasses, with graduated cross-bar, and a narrow wooden foot-rule graduated both in inches and in centimetres. A $2\frac{1}{2}$ -yard rod or tape and a 2-metre steel band measure finely graduated in inches and in centimetres. A series of graduated cones, from one-tenth inch to $2\frac{1}{2}$ inches diameter, for measuring the various orifices. A large well-graduated glass measure of about 20 oz. capacity, or even larger; this may be used for holding pieces of organs or tissue, especially if it is fitted with a ground-in stopper. A smaller graduated beaker-shaped 1 oz. glass measure, which is often useful in the removal of fluid from small sacs and pouches in the peritoneal or other cavities. Specific gravity bulb or beads.

*(*s*) A large trocar and cannula, or a flexible tube with rigid walls, to which a stomach pump may be attached, may be very useful for drawing off large accumulations of fluid, especially in cases of dropsical effusion.

*(*t*) A pair of scales with large pans, and weights from $\frac{1}{4}$ oz. to 14 lb. (1 grm. to 7 kilogrammes).

(*u*) Blue litmus papers and turmeric papers. A weak solution of iodine, made by adding 1 part of tincture of iodine to 8 or 10 parts of water. A solution of sulphide of ammonium to test for free iron derived from blood pigment, as in cases of pernicious anæmia.

*(*v*) A good magnifying glass and a compound microscope with accessories, such as slides, cover glasses, a couple of needles in handles, a small phial of physiological neutral solution (§ 36 (5)) (three fourths per cent. solution of common salt in distilled water).

(*w*) A few wide-mouthed bottles, containing hardening fluids to receive soft and delicate tissues, such as those of the central nervous system, etc. The most generally useful of these fluids is a 4 per cent. solution of formaldehyde.

For Bacteriological Examination

(*a*¹) Pacquelin's cautery, or a plumber's soldering iron (or failing these an old kitchen knife or a poker heated to redness may serve) to sear the surface of an organ or part from which it is desired to take blood, etc., for bacteriological examination.

(*b*¹) A couple of platinum wires, mounted in metal or glass handles such as are used in bacteriological work, one (the *öse*) with a loop at the end, made by turning the end of the wire round a stout knitting

needle or a thin glass rod, the other with the end beaten out to form a small spatula.

(*c*¹) Tubes of various nutrient culture media: Broth, solidified blood serum, "blood"-agar, litmus milk, potato, gelatin, glucose gelatin, and agar-agar, in tubes large enough to allow of roll cultures being made in them.

(*d*¹) Half a dozen sterile "swabs" in test-tubes, such as are used for the collection of the bacilli from the throats of patients suffering from diphtheria.

(*e*¹) Two or three sterilised Petri dishes.

(*f*¹) Half a dozen sterilised pipettes, each with an indiarubber tube and a glass mouthpiece packed with sterile cotton wool in a large test-tube. The Petri dishes, pipettes, and mouthpieces may be wrapped in tough paper before they are placed in the hot-air steriliser. The indiarubber tube should be sterilised by chemicals, not by heat.

(*g*¹) A test-tube stand.

(*h*¹) A wire test-tube crate in which is a layer of cotton wool.

(*i*¹) A couple of hypodermic syringes with asbestos pistons. The separate parts should be readily detachable, each syringe should be sterilised by dry heat and kept in a test-tube plugged with cotton wool.

(*j*¹) Three or four pairs of Cornet's forceps for holding cover glasses.

(*k*¹) A series of simple stains and differentiating reagents for immediate use. These are best kept in some form of "drop" bottle. The following are amongst the most useful:—

- | | |
|--|---|
| 1. Loeffler's methylene-blue (§ 115). | 6. Jenner's double stain for blood (§ 151). |
| 2. Carbol fuchsin (§ 120). For the Ziehl-Neelsen method. | 7. Leishman's stain for blood parasites (§ 153). |
| 3. Carbol gentian-violet (§ 119). For Gram's stain. | 8. Absolute alcohol. |
| 4. Lugol's iodine solution (§ 42). | 9. Sulphuric acid 25 per cent. solution in water (§ 183). |
| 5. Eosin (§ 132). | |

All cutting instruments must be kept perfectly clean and sharp, as nothing—except want of method—is more likely to interfere with the accuracy or the results of an examination than a set of blunt instruments. It is needless to remark, however, that post-mortem examinations have often to be made without many of the above instruments (and the lack of any of them should never be put

forward as a reason for not making such examination), but these, or decent substitutes for them, should be obtained if possible.

2. In the post-mortem theatre of a hospital, instruments, a good table, a plentiful supply of hot and cold water, and the various requisites for sponging the body and washing out the cavities should be provided. The best form of table is a slate slab 6 feet long and 2 feet broad with the corners rounded off, a bead round the edge, and so hollowed out that all fluids run to the lower or foot end, at which is a grating with a waste-pipe running to the centre, and down a hollow iron pillar, on which the table is supported, and on which it can easily revolve. The height of the table should be about 2 feet 9 inches.¹ Above the table a good "star" gas or electric light is essential for work in dark weather, and along with the gas pipe or wire a pipe for the supply of water should be brought to a point above the middle of the table; here an indiarubber hose may be attached; the hose when not in use should be kept out of the way by means of a hook, or some similar contrivance. The light and the water should both be controlled from a point within reach of the operator; this is usually done by having switches or taps similar to those used in billiard-rooms placed in the wall near the head of the table. To one side of the body should be placed a large metal basin with overflow holes about half an inch from the rim. A constant stream of water should be kept flowing through this basin; in this the operator can cleanse his hands and instruments as often as he wishes. It is most important to the operator that blood and pus should never be allowed to dry on his hands. To support the head and neck of the cadaver, a block about 15 inches long, 3 inches thick, and 9 inches broad, with half a circle with a radius of 4 or 5 inches cut out from one side, should be used: a number of blocks of a similar size, but without the excavation, and a few wedge-shaped blocks are also useful. For the examination of organs, a slate table, from 18 to 20 inches broad, with a couple of flat-bottomed slate sinks, each 3 feet long and 4 inches deep, one fitted in at about 2 feet from each end, and with 2 feet between them, is very convenient. In the sink at the left the intestines may be washed out, and a nozzle should be fitted running parallel to, and about an inch from, the bottom of this sink, at the left-hand corner. In the right-hand sink it is well to

¹ By a fulcrum and lever arrangement underneath the table, the body may be weighed as it lies in position.

have an ordinary tap to the right, and a pillar tap with a rose attached by a short indiarubber connection, about 4 or 5 inches long, so that, when not in use, it hangs vertically from an arm projecting from the back of the sink, this arm being so jointed that it can be turned out of the way of the operator. Hand-basins, with an abundant supply of hot and cold water, should also be within easy reach.

Where the examination has to be conducted in a private house, the following matters should be attended to beforehand:—

A good firm kitchen table is to be placed in the room where the cadaver is lying. (If this cannot be obtained, the coffin lid, or a door removed from its hinges and supported on a couple of chairs, is a good substitute.) The room should be well lighted, and as large and airy as possible; in a small room the windows should be thrown wide open. A piece of stout mackintosh should be spread over the table. A couple of wash-hand basins must be procured, two empty pails, a plentiful supply of water, hot and cold, a bottle of 1-20 carbolic acid (watery solution), some turpentine, and some carbolic linseed oil, 1-5. In place of the carbolic oil Dr. Lindsay Steven recommended a mixture of thymol—half a drachm, and vaseline—1 oz.; and Dr. Harris a mixture of beeswax and vaseline, worked up in a mortar in such proportions that they form a kind of paste. Clean rags, a number of newspapers, three or four sponges, a piece of soap, and several towels, should also be provided.

The hands of the operator are first thoroughly washed with warm water and turpentine; a stream of cold water is then allowed to run over them; after this they should be thoroughly anointed with the carbolic oil; or if this is not at hand, with olive oil or lard, or with one of the above mixtures. The palms of the hands should then be carefully wiped with a clean dry cloth, in order to allow of a firm grip of knives, or other instruments, being taken. From time to time during the section the stream of cold water should again be run over the hands, or they should be dipped and rubbed in the bowl of cold water placed to the side of the subject. When the section is completed, the hands are thoroughly washed, first with cold and then with warm water, soap, and turpentine, or a saturated solution of permanganate of potassium and then with oxalic acid. In place of either of these Orth recommends a dilute solution of formaldehyde as a deodoriser for the hands; when clean, some of the carbolic lotion is poured over them, and allowed to soak in, before they are wiped.

If the skin be cut, scratched, or pricked, the hands should be cleansed at once, the wound sucked, and pure nitric acid or strong acetic acid applied to it; it should then be covered with a layer of celloidin dissolved in equal parts of alcohol and ether, with good waterproof plaster (Seabury and Johnson's), or with an indiarubber finger-cap. If the hands are already cut or bruised, indiarubber post-mortem gloves, *with long sleeves*, should always be worn.

In all private cases the post-mortem examination should, if possible, be made before the body is "dressed," but if this has already been done, the operator, before he leaves, and after everything is cleaned and left in proper order, must see that it is again carefully dressed.

3. As much information as possible should be obtained from the medical attendant, the friends of the patient, and from the police, in order that search may be made for special features or lesions due to accident or disease, and, before the section is commenced, a careful note should be made of the time at which the patient died, the interval (in hours) that has elapsed between death and the examination of the body, and the external temperature and the temperature of the body. This is of considerable importance, as upon these factors depend the condition or state of preservation of the organs and the degree of post-mortem change, and, in many cases, it enables the observer to decide whether certain changes are ante-mortem, or whether they have come about subsequent to the death of the patient.

4. The body, having been placed in the supine position, with a block under the shoulders and the head hanging well down, a careful and systematic examination of the external appearances of the body must be made, and the results noted down in as clear and accurate a manner as possible. This may be done in the following order:—

Name, age, and sex (for reference), occupation, name of physician (and number of ward, if in hospital), date of death and date of examination; height (from vertex of the head to sole of the foot, in a line with the external malleolus); circumference around the shoulders; circumference of skull around frontal and occipital protuberances (in the case of a child the shape of the cranium, the various diameters, and the condition of the sutures and of the fontanelles should also be noted); the amount of adipose tissue, and the apparent state of

nutrition of the body, whether it is emaciated or there is a fair amount of subcutaneous fat; the skeletal and muscular development; and the shape and appearance generally of the head, thorax, and abdomen.

Next note the colour of the various parts of the body. Such parts as are reddened or otherwise discoloured should be firmly pressed upon with the fingers, and then examined to see whether the colour still remains *or not*. These discoloured patches should also be incised, and the colour of the tissues and the condition of the small vessels noticed. Post-mortem lividity is always most marked in the dependent parts, except where pressure is exerted from the contact of the body with the table. Unlike the colour that arises from ecchymoses, it disappears on pressure. When ecchymoses are cut into, the blood is found in the subcutaneous tissue, and cannot be pressed out. A dark fuller's earth blue or livid red colour, arranged in branching lines, is often seen on the surface, especially about the sides of the neck and on the chest and arms. This is due to decomposition of the blood in the surface veins, and the diffusion of the colouring matter of the blood into the subcutaneous tissues. Note the elasticity of the skin. A careful search must be made for abrasions or eruptions, extravasations of blood, bed-sores, ulcers, or other evidence of a diseased condition, such as pigmentation of the skin or mucous membranes, or around old cicatrices, and these must be carefully described and recorded; scars, wounds, etc., on any part of the body, and their appearance, size, and position should also be noted. Describe any jaundice or œdema that may be present.

Determine what degree of post-mortem rigidity has appeared or still remains in the various muscles of the body. This usually commences in the muscles at the side of the face and spreads from above downwards, passing off in the same order. It is always most marked in robust persons, especially those who have succumbed to very acute and rapidly fatal disease. It may appear almost immediately after death, or not for six or seven hours. Note whether there is any green coloration of the abdomen over the intercostal muscles, or in any part of the body. Such coloration, when present, points to the presence of pus or inflammatory products beneath, and is usually met with in cases of peritonitis and pleurisy, especially when the fluids have become purulent, and over abscesses. Observe the eyelids, the tension of the eyeballs, the appearance of the cornea, and the relative size of the pupils. Examine the various orifices of the body—the nose and the ears for discharges of any kind, and for foreign bodies which may have

become impacted; the mouth, about which should be noted the colour of the lips, the appearance and position of the teeth and of the lower jaw, and the relation of the tongue to these. Here also look for foreign bodies, and in the fauces and larynx. Note any increased mobility of the cervical column—fractured vertebrae. Note the condition of the breasts, the state of distension of the abdomen, and see whether there are “*linea albicantia*” or not. The organs of generation are now to be examined for any abnormality or growth, and a careful search is to be made for any evidence of inguinal or femoral hernia. (In a child it should be noted whether the testicles have descended.) The anus is to be examined in a similar manner for growths, scars, or fissures. In addition to the above it should be noted, in the case of a child, whether the anus is perforated or not, the condition of the umbilicus and the umbilical cord, the presence or absence of *vernix caseosa*, and the condition of the various epiphyses, especially of that at the lower end of the femur, which should be gradually cut away in very thin slices.

5. In making all post-mortem examinations it is necessary to have certain well-defined rules of procedure; and although, in a small minority of cases, these rules cannot be adhered to in their entirety, they nevertheless form a basis on which to work regularly and methodically. It will be found that the various sets of rules adopted by pathologists are mostly based upon Virchow's method—a method which, with more or less modification, has found almost universal favour. In the following short résumé of the various steps to be taken in conducting a post-mortem examination there is nothing original: it is an outline of a system that has been found to be exceedingly convenient, and very thorough. It is based upon that given by Virchow.¹

6. It may be laid down as a cardinal rule that, where possible, *all*

¹ Those who require a full and accurate description of the manner of conducting medico-legal sections should consult Virchow's “*Method of Performing Post-mortem Examinations, with Special Reference to Medico-Legal Practice*,” translated from the German by Dr. T. P. Smith; also “*Post-mortem Handbook for Clinical and Medico-Legal Purposes*,” by Thomas Harris, M.D. Lond., M.R.C.P.; Cuttell's “*Post-mortem Pathology*,” 1903; Rolleston and Kanthack's “*Manual of Practical Morbid Anatomy*,” 1894; Mallory and Wright's “*Pathologic Technique*,” 3rd edition, 1904; and “*A Text-Book of Pathology*” (Introductory Chapters), by the late Prof. Hamilton of Aberdeen.

the cavities of the body are to be examined, and also that they are to be examined in a regular order (head, thorax, abdomen), which order should be rigidly adhered to, unless there be very good reason for departing from it. In certain cases the abdomen or the thorax may be opened and examined first ; as, for instance, when there is good reason to suspect some grave lesion or lesions in the viscera contained within one or other of these cavities, and where the removal of some of the organs might disarrange the relative positions of the diseased parts ; otherwise, it is desirable to keep to the order and plan as closely as possible.

Orth lays it down that "the chief requisite of every exact post-mortem examination is that no part shall be displaced from its position until its surrounding parts are established, and that no part shall be taken out by whose removal the further examination of other parts is affected." An excellent guiding rule.

Keep an accurate record of every observation made, and do not trust to your memory for any detail.

In any case, before opening the head it is well to open the other cavities, and make a preliminary examination of certain of their contained viscera. This may be done as follows :—

7. Stand on the *right* side of the body, and with a strong sharp knife, held in the palm of the hand, with a drawing motion make a single incision through the skin and subcutaneous tissue of the neck, commencing at the symphysis of the chin, continuing it down the middle line of the sternum cutting down to the bone, then through the muscular wall of the abdomen, passing round the umbilicus, and extending to the pubes ;—this part of the incision not being carried deeper than the subperitoneal tissue. When the neck is not to be examined, the lower margin of the thyroid cartilage, instead of the *symphysis menti*, may be taken as the upper extremity of the incision. At one point, a little below the ensiform cartilage, make a careful incision through the peritoneum ; pass the fingers of the left hand through the opening so made :¹ raise the abdominal wall and complete the incision by cutting from within outwards, between and away from

¹ Mallory and Wright recommend that "if the presence of gas within the peritoneum is suspected, a small pouch should be formed in the first incision as soon as it has been made and water poured in. The first opening into the abdominal cavity should then be made with the point of a scalpel at the bottom of the water, through which the gas, if present, will escape."

the fingers, so as to avoid injuring any of the organs which are situated near the surface in the middle line. In order to obtain more room, cut the attachments of the pyramidales and recti muscles just above and on each side of the symphysis pubis, from within outwards, taking care not to cut through the skin. Examine the cut surface of the subcutaneous tissue and of the muscle, and note any peculiarity, such as pallor, hyaline patches (met with in enteric fever), or minute opaque white points,—encapsuled trichinae, which are found specially in the *recti* muscles; then make a careful search for any adhesion; should such be present, note its position before disturbing any of the organs. At the same time notice the relative position, to the costal and ensiform cartilages, of the liver, the stomach, intestine, and other viscera. As soon as the body is opened, and before there has been time for the oxidation of the colouring matter of the blood by the air, observe the colour of the liver. Look carefully for perforations, faecal matter in the peritoneal cavity, and constrictions of the intestine; examine the state of distension of the stomach; look for points of adhesion, perforation, or any evidence of inflammation. It is to be remembered that in all cases an external or a cut surface of an organ must be examined at once, and the colour noted, though these surfaces are also to be examined later, when the blood has become oxygenated, and has assumed the bright red colour commonly associated with arterial blood. The position of the diaphragm is to be carefully noted (the normal height on the right side is the level of the fourth rib or the fourth intercostal space; on the left side, the level of the fifth rib); and lastly, any fluid contained within the cavity is to be removed, measured, and examined, and any sign of inflammation, coagulated lymph, foreign body, tubercle, or tumour is to be examined and accurately localised. The examination of the abdomen must, for the present, be carried no further; a partial examination of the thorax must now be made.

8. The soft tissues are most easily reflected from the chest by grasping firmly with the left hand the abdominal muscles attached to the lower ribs and drawing on them whilst the knife is carried with long sweeps along the margins of the costal cartilages for some distance on to the ribs, and then, always cutting in the same direction, the whole of the costal cartilages, and 3 or 4 inches of the outer ends of the ribs and clavicle, are exposed. Then remove the sternum. With a strong cartilage knife cut through the sterno-costal cartilages as near

to the end of the ribs as possible, and cut downwards, outwards, and backwards, following the line of the attachment of the ribs to their cartilages, commencing with the second rib and passing down to the ninth, the line of incision gradually curving outwards, this curvature becoming greater as the floating ribs are reached and cut through. If care be taken to *draw* the knife in an oblique or slanting direction, the cartilages are cut through with comparative ease, but unless this direction be taken, it is often a matter of very great difficulty to divide these tough structures. When the cartilages have become ossified, it is impossible to divide them with a knife. Then, as the object is to gain free access to the chest cavity, the best plan is to divide the ribs with the saw or bone-forceps at some distance from the cartilages, great care being taken not to injure the visceral pleural sacs. (An assistant should always draw the skin over the rough exposed bones whilst the further examination is being made.) Having separated the ends of the ribs, raise the sternum with the left hand, and carefully cut away the bone from the soft tissue beneath, making one cut downwards (towards the feet) to separate the diaphragm from its attachments to the lower end of the sternum, two lateral cuts above the curve already described, and then, after feeling for any mediastinal tumour or aneurism, pass the knife upwards to the manubrium, taking care not to injure the pericardium. Cut through the cartilage of the first rib (which is very frequently ossified), and disarticulate the clavicle. To divide the first costal cartilage the knife must pass a little farther outwards than for the second rib, and, on account of the frequent ossification, it is often necessary to use the bone-forceps, even when the other cartilages have been readily divided with the knife. According to Virchow, "The best way to proceed is to insert the knife" (which should always be strong, sharp, and narrow) "with its edge looking upwards and forwards, under the cartilage of the first rib, below its inferior border, and then cut upwards and forwards." Divide the sterno-clavicular ligament, and turn the sternum backwards.¹ The next step is to open the pleural sacs; notice the position, state of distension, colour, and general appearance of the lungs, and look for any fluid, noting carefully whether it is blood-stained or not, then pass the hand between the two pleural surfaces, and make sure of the presence or

¹ I also prefer to disarticulate the manubrium sterni, as on several occasions I have seen nasty scratches inflicted by the sharp edges of the divided bone, when the sternum has been sawn from the under side and broken across.

absence of any adhesions, foreign body, tubercle, or tumour. Carefully remove and measure any fluid which may be present, just as from the abdomen. Do not for the present attempt to remove the lungs, but note the condition of the mediastinum, the size and appearance of the thymus gland, and the appearance of the vessels outside the pericardium; then open the pericardial sac by two incisions at right angles to each other, both extending from the lower and right side of the heart, one directly upwards, and the other outwards to the left side. Look for points of adhesion, especially near the great vessels: notice the appearance of the surfaces of the heart and pericardium, and remove any serous fluid which may be in normal quantity, or in greater or less excess, also look for any blood; again feel for any tumour or aneurism that may be present; and lastly, note the state of distension or contraction of the various chambers and vessels of the heart. Not until this point is reached can we commence to remove any of the viscera, as such removal is necessarily accompanied by a considerable loss of blood, which drains away from the heart, and so may alter the state of distension of the cavities of that organ, its relations to the other viscera, and to the external landmarks.

BACTERIOLOGICAL EXAMINATION

9. No post-mortem examination can now be considered to be complete without a bacteriological examination of the fluids and tissues of the body. As this examination should be made at the earliest possible moment,—before the cavities or organs are opened up in many cases, and always before any avoidable contamination has taken place,—it may be well to insert a few general directions at this point.

It is evident that inflammatory exudations, serous and purulent, should all be submitted to bacteriological examination, whilst special examinations should be made where, say, typhoid fever, cholera, epidemic meningitis, etc., are suspected. Here it is possible to give little more than general directions for the collection and examination of bacteriological material, but as no one who has not received some special training in the use of bacteriological methods will be able to make any adequate or useful bacteriological examination, a more detailed (short of complete) account is unnecessary.

General Directions for the Collection of Material

When any fluid is to be taken from a normal or an artificial cavity, heart chambers, pleura, peritoneum, abscess, etc., dissect down as near to the cavity as possible without actually opening into it. Then with the heated cautery, (§ 1 (a^1)), sear the surface of the remaining tissue and plunge into the cavity a looped platinum needle that has been heated to redness. Spread the small quantity of fluid so obtained on a cover glass cleaned by heat (§ 35*a*) and afterwards kept in a sterile glass or metal box. With the fluid that remains on the loop or with fresh material obtained in the same way, a series of sloped serum, agar and gelatin tubes, should be inoculated with a spatula-shaped needle; the needle without a fresh "charge" being used to make some ten or a dozen streaks in tubes or Petri dishes. Then with a fresh needle take a second "seeding" from one of the primary tubes, and repeat the process. A third "dilution" may be made in the same way with another fresh needle. Pure cultures may be obtained directly by this method. Broth and the various media used for the cultivation of anærobic organisms should also be inoculated and put aside for further examination. Cover glass preparations should be stained and examined at once. Cultivations from the various solid organs, liver, spleen, lymphatic glands, etc., may be obtained in the same way.

When large quantities of the material supposed to contain micro-organisms are to be taken, a "diphtheria swab" sterilised by dry heat may be used instead of the platinum needle. This swab is also useful in that it can be returned to its sterile test-tube at once, and the material absorbed kept until a more thorough examination can be made in the laboratory. We may also use for the collection of cerebro-spinal fluid, by lumbar puncture, or from the cerebral cavities, sterile pipettes with or without bulbs, as already described (§ 1 (f^1)), the fluid being blown out into sterile test-tubes, or it may be kept for a time in these pipettes until a complete examination can be made. In this latter case the fluid is drawn into the bulb, and the two ends are sealed by heat.

Sterile "fountain-pen fillers" with the glass part sterilised and kept sterile in a plugged test-tube, the indiarubber part projecting beyond the cotton wool plug should also be kept ready for use. The fluid is drawn into the tube by means of the aspirator; the whole is then

returned to the sterile test-tube. The hypodermic needle is often useful for the withdrawal of fluids from certain cavities, especially where it is to be injected directly into animals. In this case draw the fluid into the syringe very slowly in order that as little air as possible may be mixed with the fluid.

In most cases it will be found necessary to mix the fluid or emulsion obtained from cavities and organs with sterile broth or 0·8 per cent. saline solution, before injecting it into animals subcutaneously (into the mouse at the root of the tail or in the back), intraperitoneally (into rats, guinea-pigs, rabbits, etc.), or intravenously (into the marginal vein of the ear of the rabbit). For methods of plating out, and for other methods of obtaining pure cultures, *e.g.* of the cholera bacillus, etc., the student is referred to text-books on bacteriology.

Label every tube or pipette into which fluid for further examination is drawn, at once. Cultivations and other preparations should be similarly labelled.

With a pair of sterile scissors or with sterile knife and forceps, small fragments of fibrin or organs or of other tissue may be removed and introduced at once into sterile media, into subcutaneous pockets in mice (for the pneumococcus), rabbits, or guinea-pigs; or a small fragment of tissue may be broken down between two microscopic slides (kept in a wide test-tube plugged with cotton wool, the whole being sterilised by heat beforehand). From this latter broken-down tissue various media may be inoculated by means of the platinum needle. Small pieces of tissue may be conveyed to the laboratory in sterile test-tubes.

The dissection now goes on regularly, commencing with the head and neck, and then passing downwards, taking the thorax and abdomen in order.

10. Head.—After a careful external examination of the head for wounds, ecchymoses, or disease has been made, an incision is carried transversely over the vertex of the skull from behind the right ear to a similar point on the opposite side, the operator cutting *outwards* after transfixing the skin, so as to cut away no more hair than is absolutely necessary, and also to keep the edge of the knife in good order. If this be not done, the hair should be carefully parted along the proposed line of incision. Reflect the skin and pericranium over the occiput and over the forehead, exposing the occipital protuberance

and the eminences over the frontal sinuses. Then carefully examine the soft tissues and the outer surface of the bones for any abnormal appearances, or for fractures or depressions; carry the knife round the skull at the level above indicated, and divide any adherent soft tissues and the temporal muscles (or turn down the temporal muscles with their aponeuroses), and saw through the dense outer layer and part of the inner porcellaneous layer of bone in this circular direction, taking care not to allow the saw to pass through the whole thickness of the skull. During this sawing, an assistant with a skull-cap holder or with his hands protected with a strong towel should hold the head. The left hand of the operator should also be protected by a cloth. To complete the separation of the skull-cap use the mallet and steel chisel, breaking through the remainder of the inner table, unless a fracture of the bones of the skull is suspected, in which case it is better to use the saw more freely, even at the risk of injuring the membranes or the brain. In sawing through the calvaria, take care, in all cases, to go as deep as you intend at any one place before you leave it. Then, using the cross-bar of your T-shaped chisel as a lever, detach the skull-cap from the subjacent membranes. In most cases this is readily enough managed, but in persons who have suffered from chronic alcoholism, or who have been subjected to hard knocks or rough usage, it is not always such an easy matter, owing to the presence of adhesions. In children, too, where the bones are still growing rapidly, there is, almost invariably, adhesion of the skull-cap to the dura mater beneath. In such cases, it is better to combine the removal of the bony cap with the next stage and take out the brain with the skull-cap attached. Where the skull-cap can be detached, the appearances of the inner surface, any thin points or extreme thickening, and the outer surface of the dura mater and the meningeal vessels are to be noted, and the superior longitudinal sinus laid open and examined.

Next make a small opening into the dura mater on each side, just above the bony margin, and introduce at each of these openings in turn a curved probe-pointed bistoury, carrying it to the mesial line on each side, backwards and forwards, so as to divide the membrane; then with a pair of scissors cut through the attachment to the crista galli, and draw back the membrane,¹ falx cerebri and all,

¹ Hamilton recommends that the falx should not be removed from the longitudinal fissure if the brain has to be injected with a hardening fluid; the vessels are thus less disturbed.

from the surface of the brain, leaving it attached at the position of the meeting of the sinuses. Examine its inner surface, the exposed arachnoid and pia mater, and then proceed to remove the brain. Whilst these operations are being carried on, the following amongst other points should be carefully noted and recorded:—The quantity of blood in the membranes and in the cerebral cortex; the quantity and nature of the fluid in the subarachnoid space; the breadth and depth of the sulci, and the breadth of the convolutions; any flattening or depressions, discoloration, or other marked alteration, such as coagulated lymph on the surface; hæmorrhage of any kind; tubercle granulations on the pia mater, especially along the fissure of Sylvius, and at the vertex. Learn to distinguish these from the Pacchionian granulations for which they are sometimes mistaken.

With the fingers of the left hand draw back the frontal lobes, and carefully detach the olfactory bulbs from the cribriform plate with the handle of a scalpel; then, work the fingers gradually farther and farther back, so as to support the brain, and with a sharp, wet scalpel divide the optic nerves and the internal carotid vessels as near their bony channels as possible. Passing backwards, cut through the third nerves, the fourth pair as they lie in the margin of the tentorium cerebelli, and the sixth nerves, which are divided along with the tentorium. In the same manner the fifth and seventh are cut with the sharp bistoury, which is carried along the margin of the tentorium, freely dividing that membrane at its point of attachment to the petrous portion of the temporal bone. Cut through the eighth and ninth nerves, then, with a long sharp-pointed bistoury, divide the cord as low down in the canal as it is possible to reach, and carefully tilt the brain backwards from the cranial cavity with the right hand, supporting it beneath with the left. Lay it aside until the examination of the inner surface of the dura mater at the base of the skull is completed.¹ Here look for any altered conditions or new growths. Slit open the various sinuses, and note their contents (as the state of distension of the right auricle has been already observed, it is now not a matter of very great importance that the escape of blood should be prevented); examine the various vessels at their points of entrance to the skull, after which the dura mater

¹ To support the brain on the table, twist a cloth into a roll, make a circle with it, in the hollow of which the organ, vertex downwards, may rest.

may be detached with a chisel, and the bones at the base of the skull examined, especially the petrous portion of the temporal bone. See also § 30.

11. Weigh the *brain*,—average weight of encephalon, male, 49–51 oz. (1390 to 1450 grms.); female, 44–45 oz. (1250 to 1275 grms.)—and note its weight relative to that of the body. Then examine the membranes and blood vessels, especially as they lie in the fissures and sulci, and palpate the surface carefully for any abnormal depression and for any patches in which there is any altered consistency, increased hardness (sclerosis) or softening. In dissecting the brain it is necessary (as in the dissection of all the viscera) to keep two ends in view:—1st. To make as complete a naked-eye examination as possible; 2nd. to have the organ so cut up that it is possible to replace each separate part in its proper position, to enable the operator to examine the organ as a whole, or to take a small portion from any precise given area. These ends may be attained in one of several ways, but it will be well here to give two methods, by either of which this examination may be made. In using either of these methods, Virchow's cardinal rules for the attainment of the object in view should be constantly borne in mind. They may be summed up as follows:—(1) Make bold, free incisions by traction through the thickest, broadest, and longest part of the organ; (2) leave the fibrous covering of the organ, some of the vessels, or some of the parenchyma of the organ, to keep the sections attached, at one edge.

(a) Virchow's method, slightly modified.—With a long, thin, narrow-bladed knife, kept continually moistened, cut horizontally from within outwards into the hemisphere, just above the level of the corpus callosum, leaving the upper part of the brain attached to the lower, by the pia mater only, at its outer margin; make a similar incision into the opposite hemisphere. Then examine the lateral ventricles before any excess of fluid has time to escape, by cutting vertically down into the corpus callosum at a distance of one-sixteenth of an inch from the mesial plane, until at a depth of one-eighth of an inch the knife comes directly into the lateral ventricle. This incision is to be extended both backwards and forwards for some distance, in order to expose the "body" of the ventricular cavity (here also note the quantity of fluid that escapes). Then divide and subdivide, several

times, the upper portion of the cerebral hemispheres already turned outwards, always cutting from within outwards, and leaving some of the pia mater intact to hold together the wedge-shaped lamellæ. To open into the anterior horn of the ventricle cut horizontally into the frontal lobe a little below the level of the body of the cavity, removing the brain substance above the incision. The posterior horn is opened up in a similar fashion, the horizontal incision here, however, being made in a plane about three-quarters of an inch lower.

Now separate the pons, medulla, and cerebellum from the brain proper by cutting towards the mesial line in a plane the anterior border of which is just in front of the pons, the other border lying immediately behind the posterior pair of the corpora quadrigemina. A similar incision is made from the opposite side, after which the cerebellum, medulla, and the upper part of the cord may be removed, and examined later.

"Having determined the contents of the lateral ventricles, the state of their walls and venous plexus, and the condition of the septum," says Virchow, "the latter is taken hold of with the left hand, close behind the foramen of Monro, the knife is pushed in front of the fingers through this aperture, and the corpus callosum cut through obliquely, upwards and forwards, and then all these parts (corpus callosum, septum lucidum, and fornix) are carefully detached from the velum interpositum and its choroid plexus. After these two latter have been exposed, we have to examine the state of their vessels and tissue. Then the handle of the scalpel is passed from the front under the velum, which is thus detached from the pineal body and corpora quadrigemina, the state of these parts is determined, and the third ventricle now exposed."

Then open into the aqueduct of Sylvius by making a vertical incision through the corpora quadrigemina. The corpora striata and optic thalami are further examined by means of numerous incisions, "whose common starting-point is the peduncle of the cerebrum. However great the number of these incisions may be—and it is necessary here to make numerous cuts—the relationship of the parts may always be closely preserved in consequence of the connection between each separate portion and the peduncle of the cerebrum."

Cut through the peduncles of the cerebellum, after which make free

incisions into this organ in the positions already mentioned (*i.e.* to get sections having as large a surface as possible).

Treat the pons, medulla, and upper part of the cord in a similar manner, the transverse incisions to be at intervals of about from one-eighth to one-quarter of an inch, the pia mater and dura mater being left uncut on the anterior surface to bind the sections together, and keep them in position.

In some few cases, as, for example, in the brains of hydrocephalic children, where there is great distension of the ventricles, it is sometimes found convenient to do the first part of the dissection into the ventricles whilst the brain is still *in situ*, immediately after the skull-cup has been removed, and the membranes examined. In this way all risk of laceration of brain tissue and too early escape of fluid is done away with.

(*b*) The other method—one especially adapted for the exact localisation of lesions of the cortex and the secondary changes in the lower parts of the brain after it has been carefully hardened—is that adopted by D. J. Hamilton from the French school. After the brain has been removed, the carotid and vertebral vessels being injured as little as possible, it is carefully injected with Müller's fluid (§ 62) for a week or two (see "Text-Book of Pathology," vol. i. p. 57) and then further hardened in Müller's fluid for several months; or it may be injected and hardened in 4 per cent. formaldehyde. The cerebellum, medulla, and pons are then removed as in the first method, and a series of slices is made at right angles to the vertex; all the sections, from one-sixth to one-half of an inch in thickness, are made parallel to one another, and at right angles to the superior longitudinal fissure; the first section includes the tips of the frontal lobes, and the last the tips of the occipital lobes. Each slice is carefully examined, and then, by means of a small parchment or metal label, numbered and put aside for more minute examination.

A modification of this method will also be found useful in certain cases. It consists in making vertical, more or less longitudinal, sections of the injected and hardened brain, along with the cerebellum, medulla, and upper part of the cord. Where it is suspected that cortical lesions are followed by secondary degeneration descending to the cord, this method is especially useful, as by making the sections in somewhat different planes the lesion may be pretty accurately followed.

12. The directions for removing the *spinal cord* may be now given, but it is better not to proceed with this until the thoracic and abdominal viscera have been taken out, when, of course, the body is so much lighter.

The directions given by the German medico-legal authorities¹ are those which are almost universally followed.

The vertebral column is opened from behind. Place the body in the prone position with a large block supporting the thorax, and divide the skin and subcutaneous fat exactly over the spinous processes; and remove cleanly the muscles "from the sides of these latter, and from the arches of the vertebræ. . . .

"Then, by means of a chisel, or a vertebral saw, if at hand, the spinous processes, together with the adjoining portions of the vertebral arches, are to be detached and removed." A pair of strong bone forceps, especially if bent at an angle on the flat, as recommended by Dr. Savage, will prove extremely useful in removing the arch after the laminae have been partially cut with the saw or chisel. The removal is commenced as low as possible—at the second or third lumbar vertebra. "The dura mater is now exposed, and after its external surface has been examined, it is to be carefully slit open longitudinally, and the presence of any serum or extravasated blood or other abnormal matters is to be determined.

"The colour, appearance, and general condition of the posterior portion of the pia mater are next to be noticed, and the consistence of the spinal cord is to be ascertained by gently passing the finger over it.

"The roots of the nerves are next to be divided on both sides by a longitudinal incision; the lower end of the cord is to be carefully taken out, its anterior connections are to be gradually separated, and, finally, the upper end is to be removed from the occipital foramen.

"In carrying out these directions great care must be taken that the spinal cord be neither pressed upon nor bent. When removed, the condition of the pia mater on the anterior aspect is first to be examined; then the size and colour (external) of the spinal cord are to be noted; and lastly, numerous transverse incisions are to be made with a very sharp and thin knife, to determine the internal condition of the spinal cord, both of its white strands and of the grey substance." (These

¹ See Dr. T. P. Smith's translation, *loc. cit.*

incisions should not be carried through the dura mater, which should be left attached to the posterior surface of the cord in order to keep the segments in serial position. The knife should be kept constantly wetted in order to prevent sticking and tearing of the soft nervous tissue.) "The dura mater is then to be removed from the bodies of the vertebræ, and the dissector is to examine for extravasation of blood, injuries, or alterations in the bones or intervertebral cartilages." The cavity should then be carefully examined for thickening or fracture of the bone, for caries, and for evidence of pressure of any kind, such as hæmorrhage, tumours, or tubercular masses.

13. To return to the examination of the contents of the thoracic cavity. The various cavities of the *heart* may be opened separately whilst that organ still maintains its relations to the surrounding structures. It is now rotated from right to left, so that the right border of the heart may come to the front, and an incision is made into the right ventricle, commencing at the base, the knife being gradually withdrawn as it nears the apex. In the same plane make an incision into the right auricle from about midway between the two venæ cavæ to very near the base of the heart, then remove, measure, and examine the blood from the right auricle, and from the auricle examine the tricuspid opening with the fingers, taking care not to interfere in any way with the segments of the valve. In the same way, measure and examine the blood taken from the right ventricle.

To open the left auricle, make an incision, still in the same plane, between the left superior pulmonary vein and a point just on the same side of the coronary vessels (in order that these latter may be left intact).

The left ventricle is also opened by a single cut from "just behind the base" to "just short of the apex," at a distance of about half an inch from the septum. The blood is removed from these two cavities and examined as before, and the size of the mitral orifice determined (see below).

Remove the heart by dividing the inferior vena cava, the pulmonary veins, the superior vena cava, the aorta, and the pulmonary artery at as great a distance from the organ as possible. Where a bacteriological examination is to be made, as in cases of vegetative endocarditis, it is now the general practice to remove the heart, as above, before it is

incised or opened up, and, after searing a small area of the surface, to take some blood in a sterile pipette, for bacteriological examination. After removal, the heart, with its anterior surface upward, is opened up with a pair of long straight scissors or with a long narrow knife. Join the opening of the two *venæ cavæ* and continue the incision into the auricular appendage. Open the right ventricle by an incision carried through the tricuspid valve "and the wall of the ventricle, along the under surface of the right border of the heart up to the apex of the cavity"; then make a second incision from the "middle of the first, just above the insertion of the anterior papillary muscle (which should not be cut), carrying it through the pulmonary valve well over on the left side, along the left border of a narrow projecting ridge of fat tissue usually present, so as to pass between the left anterior and the posterior segments of the valve" (Mallory and Wright). Open the left auricle by an "incision joining the four orifices of the pulmonary veins and extending into the auricular appendage." To open the left ventricle make an incision through the mitral valve along the left border of the heart up to the apex, then from this point carry a second incision close to the septum parallel to the descending branch of the anterior coronary artery and on between the pulmonary valve and the left auricular appendage. Always open up the coronary arteries as far as possible. In ordinary cases where no bacteriological examination is to be made, note the size of these vessels, the thickness of their walls, any dilatation or other abnormal condition, and then carefully clear out all coagula, not only from these vessels, but also from the various orifices, and test the competence or incompetence of the aortic and pulmonary valves by means of a stream of water. This method of testing the valves has fallen, undeservedly, into some disrepute. If properly carried out, it will often prove to be of considerable value. To test the aortic opening, place the tips of two fingers—one in the right auricle and another in the left, and with the tips of one or two fingers of the other hand draw on the pulmonary artery. In this way an equal traction is made at three points, around and in the same plane as the closed valve. Allow water to run in from above, and see whether it runs away or not. If it does, and the water sinks rapidly, cut away the aorta down to within about 1 inch from the level of the valve, and note at what point the water escapes.

The pulmonary artery is to be tested in the same manner, by fixing

the margins of the vessel with the tips of the fingers of both hands, and allowing the water to run in. Take the cone diameters of the various orifices where possible. To make the examination more complete, the cavities of the heart are still further opened up; the right ventricle, by passing a pair of bowel scissors into the opening already made, and cutting towards the pulmonary artery, care being taken to avoid injuring the anterior papillary muscle of the tricuspid valve with its chordæ tendineæ. To open the left ventricle, cut with the scissors from the apex close to the septum into the aorta, passing "midway between the pulmonary orifice and the left auricle." The auricles are further opened by incisions, one running from the opening of the superior vena cava to that of the inferior vena cava, and that for the left running between the openings of the pulmonary veins. When the cavities are fully opened up, the appearances of the tricuspid and mitral valves are to be carefully observed, any thickening, contraction, roughening, or new growth, being fully noted and described. Then examine the endocardium, its colour, and the appearance of the muscle beneath, and look for clots, especially in the right auricular appendix. Observe the consistence of the muscular tissue by compressing between the fingers, and then slit open the coronary vessels with a pair of probe-pointed scissors or a probe-pointed bistoury; look for contractions, atheromatous patches, and so on. Measure the length of the various cavities, the thickness of their walls, and weigh the heart. The average weights given by different authors are—of male, from $9\frac{3}{4}$ to 13 oz., or 280 to 370 grms.; of female, 9 to 10 oz., or 250 to 280 grms.—the higher weight in each case being the more accurate. Then examine the aorta for dilatations or abnormal conditions of the inner coat especially; also examine carefully the pulmonary veins.

TABLE OF MEASUREMENTS OF THE NORMAL HEART

	SIZE OF ORIFICES	
	Hamilton.	Krause.
	(Diameter.)	(Circumference.)
Aortic orifice . . .	0·9 to 1 in.	7·7 to 8 cms.
Mitral „ . . .	1·2 „ 1·4 in.	10·4 „ 10·9 cms.
Pulmonary artery . .	1·1 „ 1·2 „	8·9 „ 9·2 „
Tricuspid orifice . .	1·5 „ 1·8 „	12·0 „ 12·7 „
Ascending aorta	7·4 „
Pulmonary artery	8·0 „ (Buhl).

LENGTH OF CAVITIES AND THICKNESS OF WALLS

Left ventricle	3 to 3 $\frac{1}{4}$ in. (Hamilton).
Wall	$\frac{1}{4}$ in. (at thinnest) to $\frac{1}{2}$ in. (at thickest). „
[Without trabeculæ]	7 to 10 mm. (Orth)].
Right ventricle	3 $\frac{1}{16}$ to 3 $\frac{3}{8}$ in. (Hamilton).
Wall	$\frac{1}{8}$ in. (over all). „
[Without trabeculæ]	2 to 3 mm. (Orth)].

14. *Lungs*.—After careful examination of the serous surfaces, which are usually somewhat altered if there is any fluid present, a careful search is made for any abnormal appearances. Should there be any considerable quantity of blood in either of the pleural cavities, the aorta should be examined for aneurismal dilatations. This should also be done where there has been any evidence of pressure on either the lungs or the bronchi. To remove the lungs, seize the upper lobe with the left hand, and cut from above downwards and backwards through the bronchi and vessels as far as possible from the point where they enter the lung, and then through the broad pulmonary ligament. When the base of the lung is adherent to the diaphragm it is well to remove the two together, carrying the incision through the diaphragm at its insertion into the ribs. The left lung should first be removed and then the right, each being placed on its own side of the body on the table. Average weight—in the male, right lung, 24 oz. (680 grms.), left lung, 21 oz. (600 grms.); in the female, right lung, 17 oz. (480 grms.), left lung 15 oz. (420 grms.). Where there are adhesions, localised or general, which cannot be broken down with the fingers, the costal pleura must be dissected away along with the lungs. Whilst breaking down these adhesions, or when working in the thoracic cavity, it is well to get an assistant to hold the reflected mass of skin and muscle over the ends of the ribs, especially when the cartilages are ossified, or when the saw has been used. Examine the outer surface of the lung for fibrinous exudation, colour, minute hæmorrhages, fibrous adhesions, fibroid or cancerous nodules, excessive pigmentation along the lines of the interlobular septa, miliary tubercles in the same position, emphysematous bullæ, gangrenous sloughs, consolidated patches, cicatrices, or any abnormal appearances, and note the colour of any consolidated patches, whether grey (catarrhal), yellow or caseous (tubercular), or red (infarction). Note whether these latter are wedge-shaped (at the

free border) or rounded (in the substance of the lung). This can only be made out after the lung has been incised. To do this make a long free cut from apex to base, commencing at the outer rounded surface, and passing to the root, so as to bisect the bronchial glands, leaving the two portions attached by the vessels and bronchi forming the root of the lung. Then examine the cut surface, note the amount of blood exuding, and how much may be squeezed out on pressure; note also how much air and serum may be squeezed out (œdema), and the colour of the serum (dirty brown in brown induration, bloody in acute congestion). Examine scrapings and consolidated patches, etc., as seen on the surface; further examine the consolidated patches, and see if there are any cavities in them. Note the number and extent of these if present, especially when they are near the apex. Examine the walls of these cavities and the pleura above them; note their relations to the bronchi. Try the specific gravity of any consolidated or suspicious patches by placing them in water and noting whether they float or sink.

Observe the condition of the fibrous septa and of the pleural covering of the lung, the *bronchial glands* (enlargement, caseation, pigmentation), and then with a pair of scissors slit open the branches of the bronchus and pulmonary artery; note the appearances of the lining membranes of these channels, and look for foreign bodies, clots, new growths, or any obstructive mass.

15. It is seldom necessary to examine the parts about the side of the *face* and *ear*; but when this is necessary the various structures may all be exposed by continuing the vertical incision over the skull, down behind the ears to the neck, throwing the skin forward, so that it may be replaced at the conclusion of the dissection. (§ 30.)

16. In the *neck* open the carotid sheath at once, after reflecting the skin, muscles, and fascia of the side of the neck and the floor of the mouth, and examine the vessels, the vagus, and the sympathetic ganglia: then dissect out the larynx, œsophagus, and pharynx *en masse*, and remove them along with the tongue and soft palate by cutting through the muscles passing from the hyoid bone to the lower jaw, close behind the symphysis menti, and cutting along the rami back to the base of the skull. Free the upper part of the pharynx behind, draw forward the tongue below the jaw, and then cut through

the soft parts immediately behind its hard attachment, and remove the pillars of the fauces, the floor of the mouth being thus entirely detached. With the bowel scissors open up the œsophagus from behind; the larynx and trachea are also to be cut up from behind, care being taken to avoid injuring the œsophagus. The epiglottis and vocal cords can then be examined. Open the Eustachian tubes and examine for new growths and the condition of the mucous membrane; then examine, in turn, the thyroid and salivary glands, the tonsils, and the cervical lymphatic glands.

Complete the examination of the abdominal cavity.

17. Take out the *omentum*, and sever it from the transverse colon, as close to the gut as possible, noticing any abnormal growths or appearances, redness, coagulated lymph (fibrin), colloid mass, tubercle, thickening, contraction, or constriction of the intestine.

18. After noting the position and taking measurements whilst the organ is still *in situ*, remove the *spleen* by cutting through its vessels and peritoneal attachments. Weigh the organ (normal weight—male, $5\frac{1}{2}$ oz., or 156 grms.; female, $4\frac{3}{4}$ oz., or 136 grms.) and examine the capsule for thickenings or alterations in colour. Make a free incision through the thickest and longest part; note the colour, consistence, amount of blood exuded, and the appearances of the trabeculae and the Malpighian bodies. Pour a watery solution of iodine over the surface, and examine again, especially the Malpighian bodies. If there are any cicatrices, swellings, or other evidences of infarction or tubercle, make other incisions in various directions.

19. Remove and examine each *kidney* separately, first the left, and then the right, placing each on its own side of the body; take out at the same time the corresponding suprarenal capsules and the semilunar ganglia. To remove the kidney make “a vertical incision through the peritoneum, external to and behind the ascending or descending colon; the intestine is to be pushed aside, and the kidney detached from its connections,” by a single cut near the hilus. Remove the fat and other tissue from the capsule and weigh the organ ($5\frac{1}{4}$ oz., or 150 grms. in the male, a little less in the female; left a little heavier than the right), and examine the outer surface for evidence of surrounding inflammation, then make an incision from the convex

outer border of the organ down to the pelvis; note the relative thicknesses of the medulla and cortex,—normally about 7 : 3 (Hamilton gives it as 3 : 1). If there is any marked deviation from these proportions, examine the organ most carefully, and notice the amount of blood exuding from the cut surface, the colour of the cortex and of the medulla, especially at the bases of the pyramids. Then strip off the capsule, and see whether it is thickened, adherent, or laminated. Examine the surface for “granulations,” cysts, tubercles, cicatrices, depressions or elevations, or persistent marking out of the lobes; note the state of distension of the *venæ stellatæ*, the colour of the surface, and so on, after which try the consistence of the organ.

Note the size, patency, and thickness of the walls of the arteries in the boundary area, the regularity or irregularity of arrangement and size of the Malpighian bodies, the appearances of the interlobular vessels in the cortex and the straight vessels and tubules in the pyramids, noting any changes or accumulations in the tubules, especially near the apices of the papillæ; look for cysts, and then examine the condition of the mucous membrane of the calyces, pelvis, and ureter, the latter of which should be slit up with a probe-pointed bistoury, unless it is deemed desirable to remove, together, the kidney, bladder, and ureters for more careful examination outside the body.

Stain a section with a watery solution of iodine (§ 1 (*u*)), and examine the Malpighian bodies and straight vessels.

In examining the kidney always begin at the capsule and work systematically towards the pelvis.

20. The *suprarenal capsules* are to be described as to size, colour, consistence, and appearances on section (induration, caseation, waxy appearance—for the latter apply the watery solution of iodine); examine along with them the *semilunar ganglia* of the corresponding sides; any firmness of these ganglia is to be noted, also any signs of inflammatory thickening or pigmentation, where such are present. Preserve both structures for microscopic examination.

21. The *bladder* is next opened *in situ*, and any peculiarity of the mucous membrane—pouches, thickening of the walls, papillomatous growths, deposits of ammoniacal phosphates—observed. Remove the contents of the pelvis, and examine the *prostate*, *vesiculæ seminales*, and *urethra* for signs of inflammation, enlargement, or stricture;

the *testicles* and *spermatic cord* are also examined for caseation enlargement, or other changes.

22. In the female, look for evidence of injury to the wall or peritoneal covering of the *uterus*; remove and note the condition of the *vagina*, search for ulceration, or new growths on the *os uteri*. Examine the uterus, noting its size, the thickness and consistence of its muscular wall, the condition of the mucous membrane, the corrugations (*arbor vite*) at the neck, the appearances of the vessels, and also any new growths, and their positions; note the condition of the broad ligaments and the Fallopian tubes; and look for corpora lutea, cicatrices, cysts, or new growths in the ovary.

23. Next cut out the *rectum* after placing on it a couple of ligatures; slit it up, and examine its mucous membrane; look for fissures, stricture due to new growths or other causes, for varicose conditions of the veins, etc.

24. At this stage Virchow insists that the *duodenum* and *stomach* should be examined for adhesions, perforations, or any other abnormal appearances, and should then be opened *in situ* by an incision (made with a pair of scissors) running longitudinally along the anterior surface of the duodenum and the greater curvature of the stomach. In all cases, however, where it is suspected that traces of poison may be found in the stomach, the organ should be removed before it is opened, and at as early a stage of the examination as possible. A couple of *double* ligatures are applied, one round the upper end of the *œsophagus*, the second round the lower part of the duodenum. The interval between the parts of each double ligature should be at least an inch, in order that there may be no danger of the string slipping when the tissues between them are cut. Remove the stomach, with its contents, and then empty these contents into a clean bottle, after cutting the ligature at the duodenal end; the stomach may then be examined. It is sometimes recommended that this method should be adopted in every case, and it certainly has the great advantage of cleanliness. Hamilton's plan of first making a short opening along the lesser curvature and then taking the cone diameters of the two orifices is one to be commended. It may be carried out either when the stomach is opened *in situ* or after it has been removed. Determine

the contents of the duodenum, "above and below the papilla biliaria; this papilla should be examined, and its contents gently pressed out; then, by pressing on the gall bladder, we should determine the presence or absence of obstacles to the flow of bile; and, lastly, the *ductus communis choledochus* should be slit up. Then the *vena cava* should be examined, especially where death from suffocation is suspected, and, all this having been done, the liver should be removed. It is quite useless to pass a probe along the gall duct, for our being able to introduce a probe into the orifice is no evidence whatever that the portio intestinalis was pervious during life."

The *stomach* should be examined at the same time as the duodenum, and any thickening of the pylorus, or congestion or ulceration of the mucous membrane noted.

25. Many pathologists remove the *liver* first, but it is better, in many cases, to leave it until this stage, in order that the relations of the organ itself, and of the gall bladder and duct to the stomach, duodenum, and head of the pancreas may be determined. To free it carry the knife through the arch of the diaphragm along the left border of the liver, then pulling the organ forward, sweep through the falciform ligament, and cut through the remaining attachments to the diaphragm, posteriorly. Slit open the gall bladder and look for watery or inspissated bile, gall stones, or any other abnormal condition; weigh (average weight—in the male 48–50 oz. = about 1360–1420 grms., in the female 41–42 oz. = about 1160–1200 grms.) and measure;¹ note the shape, consistence, and resistance to pressure, and examine the external surface for thickenings or any abnormal appearance. Make transverse sections from right to left through the substance of the organ, leaving the sections united by one edge at the under surface of the organ; note the toughness of the tissue as the knife passes through it, and test its consistence and friability with the fingers; observe the amount of blood contained, the size of the vessels, the appearance of the capsule on section, the amount of

¹ Mallory and Wright give the liver measurements as follow:—

Length from right to left	25–32	cms.
Width of right lobe	18–20	„
„ „ left	„	8–10	„
Vertical diameter of right lobe	20–22	„
„ „ „ left	„	15–16	„
Greatest thickness	6–9.5	„

connective tissue, the colour and appearance of each zone of one of the lobules (before and after the addition of iodine solution), also the size of the section of a lobule (about $\frac{1}{16}$ – $\frac{1}{32}$ of an inch); look for new growths, such as cancer, sarcoma, or tubercle.

After the removal of the liver, the stomach and the duodenum—if not already removed—may be drawn upwards and excised by cutting parallel to the vertebræ through the head of the pancreas, and then pulling forward and cutting through the various posterior attachments.

26. Then reach the *pancreas* by tearing through the omentum between the stomach and colon, thus making an opening into the lesser peritoneal sac. Examine this organ, especially at its attachment in the curve of the duodenum, for tumours or cysts, which are usually found in the head,—the part that lies in the curve,—and take out the semilunar ganglia, if this has not been done when the kidneys were removed; it is to be remembered that in some cases it is much easier to do it at this stage, when the pancreas has been got out of the way, than earlier. Weight of pancreas, $2\frac{3}{4}$ – $4\frac{1}{4}$ oz. (80–120 grms.).

27. The *mesentery* and *intestines* are examined *in situ*, along with any adhesions, new growths, or enlarged glands; the condition of the *vessels* and *lymphatics* should be observed; then, taking hold of a loop, cut with a sharp knife through the attachment of the mesentery close to the intestine. The two extremities of the intestine have already been tied, and nothing remains to be done but to put on a double ligature at about 1 foot above the large intestine, and draw the intestine from the abdominal cavity; cut the ligature and send a stream of water through the intestine to wash out its contents, unless there are special reasons for examining these in the different parts of the intestine; and then slit up the bowel with the bowel scissors, taking care to cut through the walls at the point of attachment to the mesentery. Examine the mucous membrane for thickenings or changes in its various structures, congestion, ulceration, sloughing, perforation, and so on; at the same time examine the mesenteric attachment for tubercle nodules along the lines of the lymphatics; typhoid swellings and ulcers are to be specially looked for, just above and below the ileo-cæcal valve, whilst the valve itself should always be most carefully

examined for tubercular ulceration, and, "in every case of peritoneal inflammation examine carefully the vermiform appendage." Apply iodine to the mucous surface.

28. Lastly, examine the *retro-peritoneal glands*, *thoracic duct*, *receptaculum chyli*, *aorta*, *vena cava*, and the large trunks going into the pelvis; and also, if necessary, the sympathetic nerve trunks.

In certain cases other structures have to be examined, or more particular attention has to be paid to special parts; but the necessity for doing this will be indicated by the clinical history of the case. In such cases special dissections must be made.

29. Where it is necessary to remove the whole eye two saw cuts should be made, one vertically downwards through the frontal bone and the roof of the orbit, in a line corresponding to the inner side of the orbit as one extreme, and the inner side of the optic foramen as the other, the other line being drawn from the outer side of the orbit to the outer side of the optic foramen. As soon as the bone is cut through, a sharp tap forward behind the frontal bone will cause the horizontal plate to tilt up; this allows of a complete dissection of the eye being made. The ring around the optic foramen may be left *in situ* by chiselling through the thin plate of bone that lies in front of it. If the whole eye is removed, however, the face is somewhat disfigured, and as in most cases it is quite sufficient to remove the posterior half of the globe, all that is necessary is to smash in and remove the thin orbital plate of the roof with a chisel or a pair of strong bone-forceps. The muscles and nerves can then be dissected out, and the posterior half of the eye may be removed with a pair of sharp-pointed scissors, the parts being held in position with a pair of forceps. A scrap of dark-coloured cloth held in position behind the pupil, with cotton wadding, prevents any disfigurement.

30. The temporal bone with its petrous portion containing the internal ear may be taken out and examined after removal of the brain by stripping off the dura mater from the base, dissecting off the skin and muscle, detaching the external ear from the bone and disarticulating the jaw; then taking the margins of the temporal bone as the base of a pyramid, the apex of which is a little beyond the inner extremity of the petrous portion, two saw cuts are carried

almost vertically downwards so as to bound the pyramid; then with a bone chisel and mallet the whole temporal bone may be removed, after which it may be softened in a decalcifying fluid, or the middle and internal ear may be dissected out with a small saw, a pair of sharp well-fitting bone-forceps, and a sharp gouge and chisel.

Mallory and Wright recommend the following method for the examination of the petrous bone after it has been removed as above:—"Chisel off the tegmen tympani so as to get a view of the middle ear. Next remove the lower wall of the external meatus, so as to expose the outer surface of the membrana tympani. Finally divide the petrous bone with a fine hair-saw by an incision starting in at the styloid process and coming out at the carotid canal, parallel to the crest of the pyramid of the petrous bone.

"This incision divides the cavum tympani into halves. In the lateral half can be seen the membrana tympani with the hammer and the anterior half of the mastoid cells. In the median half are the labyrinthine wall of the cavum tympani with the stapes and the posterior half of the mastoid cells. It is best to remove the anvil before sawing through the bone." Open up the Eustachian tube from the middle ear.

31. The following method of examining the nose is one that I have sometimes used since I read Dr. Harris' little hand-book, from which the description is taken:—

"After the brain has been removed, and the base of the skull has been examined, the body of the sphenoid bone, a little in front of its line of union with the basilar portion of the occipital bone, is divided transversely with the aid of a chisel, and then by means of a small saw the base of the skull is divided along a line running on either side from the extremities of the incision in the body of the sphenoid, through the middle fossa on the outer side of the cavernous sinus, and thence forward through the lesser wing of the sphenoid to the anterior fossa, where the inner part of the orbital plate or the frontal bone on both sides is divided as far as its anterior extremity, and then the extremities of these incisions are united by a transverse one across the front part of the perforated plate of the ethmoid bone. We are then enabled, by means of a chisel and a pair of bone-forceps, to remove the portion of the base of the skull included between the lines of incision, and to examine the interior of the nasal cavities."

AVERAGE WEIGHTS OF ORGANS

Table used in the Post-mortem Room of the Royal Infirmary, Edinburgh

	MALE.		FEMALE.	
	lbs.	oz.	lbs.	oz.
Human brain	3	1½	2	1½
„ heart	11	...	9
„ lungs	2	13	2	...
„ liver	3	5	2	12
„ pancreas	3	...	2¼
„ spleen	6	...	5½
	<i>Right.</i>	<i>Left.</i>	<i>Right.</i>	<i>Left.</i>
	oz.	oz.	oz.	oz.
„ kidneys	5¼	5½	4¾	5

32. Mallory and Wright make a number of “Suggestions to Beginners,” which I take the liberty of introducing bodily, as they give in concise form most valuable instruction to the tyro. They say: “In a case of *general miliary tuberculosis* the older focus from which the organisms have spread must always be found. Look especially for tubercular thrombi in the pulmonary veins as a frequent source of the general infection.

“In a case of *embolism* hunt for the thrombus, bearing in mind however, that the whole of a thrombus may become free and form an embolus. An arterial embolus may be due to a venous thrombus, in which case it must have passed through an open foramen ovale, except in the case of thrombi of the pulmonary veins.

“In acute *peritonitis* always seek for a source of infection (appendix, female genitals, gastro-intestinal tract, etc.). It cannot always be found.

“In *hæmorrhage from the stomach* associated with the cirrhosis of the liver, look for rupture of dilated œsophageal veins.

“In cases of more or less *sudden death*, especially if preceded by signs of asphyxia, always examine the pulmonary artery *in situ* for possible emboli,” by thrusting a sharp-pointed scalpel through the artery just above the valve, and cutting upward until the branches to the right and left lung are reached. This incision may also be continued in the

opposite direction towards the heart. "In cases of *instantaneous death* examine the coronary arteries."

To these suggestions may be added :

Always examine the fauces for *foreign bodies*.

Remember that acute peritonitis is one of the most fertile sources of septic poisoning amongst pathologists.

In cases of hæmorrhage from the bowel, examine the mesentery and mesocolon for thrombi, also make a careful search for an abdominal aneurism.

Remember that ecchymoses may be the result of, amongst other causes, septic mischief, scurvy, leucocythæmia, or phosphorus poisoning.

CHAPTER II

PATHOLOGICAL HISTOLOGY

33. *Instruments required.*—To the student entering upon this department of pathological investigation, who has not already made himself, to some extent, master of histological methods, a few words are necessary as to the selection of the apparatus used in carrying on microscopic work.

First, as to the microscope itself; this should, if possible, never be bought without the assistance or advice of some one well qualified to decide on the merits of the instrument.

It may help the student in his selection, however, if a short description of a good compound microscope, such as is suitable for pathological work, be given.

The pedestal must be firm and steady, either a tripod with a good broad base, or a horse-shoe. Fixed into this is a column of sufficient thickness to ensure strength, and jointed just below the stage, to allow of the whole instrument being inclined, or even bent to a right angle, if necessary; the tripod should be so based that the stand remains perfectly steady in this position. The stage should be immovably fixed into the pillar at a convenient distance from the base, *i.e.* not so high that the arms may not rest on the table when the fingers of the left hand are moving the slide over its surface. Unless a mechanical stage is to be attached, the transverse diameter of the stage should not be greater than the length of the ordinary glass slide—3 inches. The antero-posterior diameter must not be less than $2\frac{1}{2}$ inches. On each side of the pillar there should be a brass clip fixed into holes in the stage. These are of use in fixing an object in any desired position for examination, and—when there is no mechanical stage—for controlling the movement of the slide when a high power is used.

A mechanical stage adds enormously to the expense of the instru-

ment. Now, however, that so much bacteriological work for which high magnification is essential, is done, it is advisable to acquire a microscope to which such a stage and a substage may be added, but for continued work, the manipulation of the screws tires the hand so much more than does the movement of the slide by means of the fingers that for the present the mechanical stage may be omitted. In the centre of the stage is an aperture about five-eighths of an inch in diameter. The under surface of the stage should be recessed, so that a domed Iris diaphragm when closed may come almost to the level of the upper surface of the stage. Although it is scarcely necessary to obtain a condenser for histological work, it must be remembered that at a later period bacteriological investigation will have to be entered upon. It is well therefore, whatever microscope be obtained, to have some arrangement to which a condenser may be fitted. The best arrangement is a light ring substage which will receive a swing-out condenser with an Iris diaphragm beneath; this substage should have a rack and pinion adjustment. It adds slightly to the cost of the microscope at the outset, but the instrument is much more valuable at a later stage.

Under the stage, and fixed to the pillar above the joint, or to the bar on to which the substage is to be fixed, is a movable mirror, which can be focused on the object. For ordinary work a slightly concave reflecting surface is used, but for work with very low powers, or with an achromatic condenser, a plane mirror is necessary. These mirrors are used for the illumination of objects by transmitted light, or light sent through the object to the eye of the observer: it is therefore especially useful in the examination of transparent objects, which form by far the greater proportion of those which fall to be studied by the pathologist. In most cases the light is passed through at right angles to the plane of the section; but where the tissues are very delicate or very transparent it may be thrown from beneath, obliquely; a shadow picture is thus produced, and even delicate structures are thrown into relief.

The part of the microscope above the stage is the more important. Of this it will be well to describe two forms, and point out the special advantages of each.

The first form, the smaller continental model, has an arm fixed at right angles to the pillar; into this arm is screwed a hollow split tube, about $2\frac{3}{4}$ inches in length; working in this is a telescopic tube, com-

posed of two segments, measuring, when closed, about 5 inches, and when drawn out to the full extent, 7 inches in length. In this case the coarse adjustment is effected by giving a spiral motion to the telescopic tube in the split tube. When the parts are kept *perfectly clean*, this adjustment answers admirably, even with moderately high powers; but when the tubes are allowed to get at all dirty, the force exerted at the end of the lever is apt to shake the joints of the microscope. This is the simplest and cheapest form of coarse adjustment, and, where no nose-piece is used, it is also the best and the most convenient, as the tube can be quickly withdrawn when the lenses are to be changed.

Perfect cleanliness is all that is needed to keep this part of the microscope in good condition; and it is to be remembered that on no account is oil to be used—it merely clogs the tubes by accumulating in the slits. The sliding parts should be polished from time to time with a *little* powdered French chalk, which must afterwards be carefully removed.

The fine adjustment is made by means of a milled head placed at the upper end of the pillar. If this be efficient the screw should work perfectly steadily, and not “lose time”—*i.e.* the slightest turn of the screw should alter the focus, and the alteration should be smooth and steady, and not in jerks. Neither the coarse nor the fine adjustment when working should give rise to the slightest lateral movement of the image in the field.

The feature wherein the second form differs from the first is in the method of making the coarse adjustment, which is effected by means of an oblique rack and pinion. This, like the fine adjustment, should be attached to the pedestal, and not to the end of the arm which supports the body of the microscope. The pinion is turned by means of “milled heads”; it should work smoothly and without any “loss of time.” In the English model the tube is usually 10 inches long, and the lenses must be specially corrected for that length.

To the body of the microscope may be attached a bull’s-eye condenser, consisting of a plano-convex lens, at the end of an arm which is fixed by a universal joint to a movable split ring fitting around the split tube; this may be fixed to a separate pedestal or standard. By this condenser light may be focused directly on to the object under examination,—such as a section of waxy liver stained with iodine, or an opaque object; from the section it is reflected to the eye.

(Care must be taken to have the condenser at right angles to the rays of light.) In some microscopes the condenser is fixed to the stage, where, however, it is usually in the way.

The optical parts of the microscope—the eye-piece and the objectives—are naturally the most important. In selecting these, take care to obtain such as will give a magnification of about 50 for the low power, and 300 with the higher combination. In some of the continental microscopes, these are approximately given with a No. 3 eye-piece, and objectives Nos. 3 and 7; in the microscopes of English make, ocular No. 3, with five-seventh inch to 1 inch and one-sixth or one-seventh inch (80° – 100° angle of aperture—Hamilton) objectives; and in Zeiss's microscopes, ocular No. 3, with objectives A and D. Lower and higher powers may afterwards be obtained for special work, but the above lenses will be quite sufficient for ordinary histological investigation. In selecting the lenses, note the following points, testing by means (1) of a thin film of blood, and (2) salivary corpuscles. The lenses should be perfectly achromatic; the low power should have good definition and a *flat field*. In regard to the low power this last point is of special importance, as with it the general outlines of the structure are first examined, and it is necessary to have as much as possible of the tissue under observation, in focus, at one time.

Focus the blood corpuscles in the centre of the field, and then observe whether those at the margin of the field are equally distinctly seen.

The higher power should have *good definition*; the field should also be flat; but this is not a matter of such great moment as the clear definition of delicate structures, such as those seen in a well-stained salivary corpuscle.¹

¹ The demand for good and cheap microscopes, at prices ranging from £3, 3s. to £5, 5s., is now very great, and a considerable number have lately been offered to the student. From actual experience the author can recommend almost any of the makes, either English or continental, as being good and reliable.

Of the more expensive microscopes the best are those made on the pattern early adopted by Zeiss, ranging in price from £7, 10s. to £15. The other appliances, optical and mechanical, may be had up to any sum that the purchaser may feel inclined to expend. For high power work the best objectives are an F (one-eighth inch) and the one-twelfth inch oil immersion. Most of the English makers have made great efforts to meet an increasing demand, and they may be relied upon to supply stands of which the workmanship is thoroughly good and the optical appliances of the first quality. Several continental makers also make good higher priced microscopes. The high power lenses made by most of the English makers are excellent both for flatness of field and sharpness of definition.

34. The following most useful accessory apparatus may, with advantage, be procured :—

A double or triple nose-piece, properly centred. This will ensure a great saving of both time and trouble, especially where the rack and pinion coarse adjustment is used. Zeiss's new sliding apparatus is equally convenient where the rack and pinion movement is used, and much more so where the adjustment is made by means of the sliding tube.

An achromatic substage condenser by one of the English makers, a Powell and Leland's oil condenser, or an Abbé's illuminator hinged so that it can swing out and in easily, is essential when micro-organisms are to be studied.

A paraffin lamp, with a blue glass chimney, or, what answers equally well, an Argand gas burner fitted with a blue glass chimney. (This combination may be obtained for about 7s. 6d.)¹

A micrometer eye-piece and a stage micrometer.²

A camera lucida, Abbé's, made by Zeiss, or one made by Nachet of Paris.

A warm stage or a constant temperature hot-box to enclose the microscope (Zeiss).

DIRECTIONS FOR WORKING WITH THE MICROSCOPE

35. Clean the front of the objective and both lenses of the eye-piece with a piece of soft chamois leather, a silk handkerchief, or a camel-hair pencil, using, if the glasses are greasy, a little weak ammonia, benzine, or xylol. Take out the draw-tube, screw on the No. 3 or low power objective, put in the No. 3 eye-piece, close the telescope tube and replace the draw-tube; then bring the lens down nearly to the level of the stage, and illuminate the field by reflecting the light upwards, from the substage mirror, through the largest aperture of the diaphragm. The best light that can be obtained for the purpose is a north light, not too bright, reflected from a bank of white cloud; for night-work, a lamp as already described may be used. A screen of white tissue paper or of ground glass placed before the lamp will

¹ A small electric lamp which is now made can be fitted under the stage; it gives a good white light, and answers admirably.

² Directions for determining the magnifying power of a lens or a combination of lenses, and for measuring the actual size of cells and bacteria are given in all the technical works on the microscope.

modify both the heat and the glare of the light ; whilst, if the flame be too yellow, a globe containing a solution of ammoniated sulphate of copper may be used. When looking through the eye-piece keep both eyes open. If any specks are visible in the bright field, turn the eye-piece, and if the specks move, they are on the eye-piece and not on the objective. If there is simply blurring or cloudiness in parts of the field, the objective is still dirty, and should be more carefully cleaned. Place a slide on the stage, gradually draw the tube *upwards*, or work it upwards with the coarse adjustment, moving the slide over the stage with the left hand, and look down the tube, until the specimen comes into view in the bright field. Then with the fine adjustment bring the object accurately into focus.

By commencing with low powers near the stage (about a quarter of an inch away) there is less danger of bringing a very low power, say, a 2 or 4-inch objective, down on the slide.

In all cases, the general features of the object should first be studied under the low power ; from this preliminary study much is to be learned.

Place in the centre of the field any part of the object which is to be examined further, and screw on the high power lens, or turn round the arm of the nose-piece to which the high power lens is attached. Centre a small aperture of the diaphragm. The objective is then brought to a distance of a quarter of an inch from the stage, and is gradually brought *down* by means of the coarse adjustment to the point at which the outline of the specimen may be seen (the directions given above as to looking through the microscope whilst the object is being focused still being borne in mind) ; then focus more carefully with the fine adjustment, and bring into use the aperture of the diaphragm, which, whilst allowing the passage of sufficient light, enables you to obtain the sharpest definition. It must be remembered that *it is always necessary to use a smaller aperture when a specimen is unstained than when it is stained*. The beginner will from time to time bring the high power lens down into the Canada balsam or other mounting fluid, unless very great care be taken to attend to the directions given above. When this occurs, it is well to remember that the Canada balsam may be dissolved off by means of a drop of clove oil or xylol, which should, however, be removed at once, or it will loosen the lenses, which are usually "set" in Canada balsam.

In reading the above directions, it will be noticed that nothing has been said about changing the eye-piece. This is intentional, and the

student will find that it is better to accustom himself to the use of a single eye-piece, and to alter the magnifying power by means of the objectives, rather than by changing the eye-piece. With a *perfect* lens, any eye-piece may be used, but where there are the very slightest defects in the lens, these are, of course, magnified by the higher eye-pieces, which magnify only the image given by the objective. The same remark holds good as regards the lengthening of the tube. When possible, work with the shorter tube, for, although greater magnifying power is obtained when the tube is drawn out, the definition is not so good, except with first-class lenses, and in a very strong light.¹

The student should accustom himself to work with the microscope in a vertical position, as the fingers can move the slide much more steadily over a level stage,—fluids should always be examined on a horizontal stage. With the high power, the clips gently pressed down on to the slide will prove of very great service in controlling its movements. A list of the apparatus and reagents required is given on page 153 *et seq.*

35a. Before setting to work, see that both slides and cover-glasses are perfectly clean. Slides as supplied are, as a rule, pretty free from grease or hard film, and can be readily cleansed by thoroughly washing them in clean water, and drying them carefully with an old cloth; new cover-glasses, however, are sometimes coated with grease, or with a hard film, which cannot be got rid of by water alone. To cleanse them, put them into a shallow glass or porcelain dish, and cover them with a mixture of strong sulphuric acid 60 parts, potassium bichromate 60 parts, and distilled water 1000 parts (van Ermengem's fluid); boil for an hour, adding fresh solution as it evaporates; wash well with distilled water, and keep in absolute alcohol. As they are required for use, transfer them from the bottle with clean forceps to a clean piece of fine wire-gauze fixed on a frame so as to form a kind of flat spoon and burn them over a Bunsen flame. Once clean, they should always be held by the edges; they should never be laid down flat, but should be tilted up against some convenient object, such as the microscope or the reagent stand, until required.

¹ With the apochromatic lenses as now constructed this does not hold good, but as the student is not likely to use these except when he has become accustomed to the use of the microscope, it is not necessary here to go into that question.

EXAMINATION OF FRESH TISSUES

36. For the pathologist, even more than for the student of normal histology, it is necessary to examine tissues in a fresh condition. In making such examinations, the tissues must be bathed in a medium which will not change either the appearances or the vital properties of their various elements more than is absolutely necessary, and where possible, tissue elements should be examined in the fluid in which they are normally bathed. Pus, blood, fluid secretions, and sediments usually contain sufficient fluid to allow of the corpuscles being easily mounted; and when mounted, the corpuscles undergo comparatively little change, until the quality of the fluid is altered by evaporation, or until the altered temperature begins to tell upon them. Where larger sections or fragments are to be examined, or where the fluid is too thick, it is necessary to extemporise a neutral medium in which to bathe the tissue. In the case of gland tissue, nerve fibrils, splenic pulp, and similar delicate and unstable tissues, the use of such a fluid is essential. Any of the following may be used:—

1. Aqueous humour, after puncturing the cornea with a triangular knife, taken from the anterior chamber of the eye of a newly killed ox. This, of course, is available in small quantities only.

2. Serous fluids, such as that taken from the pericardial sac (which is always procurable in the post-mortem room), hydrocele fluid, amniotic fluid, or even blood serum (which are not so readily obtained).

3. An artificial serum may be made by adding to 1 part of egg albumen, 9 parts of neutral salt solution (see 5).

4. To any of these serous fluids, iodine may be added to form *iodised serum*. It is prepared by adding

1 part tincture of iodine to
100 parts of serous fluid.

To each ounce of the fluid add a couple of drops of carbolic acid, and filter. This may be kept for some time, but should be prepared fresh whenever opportunity occurs. Its advantages are that it alters the tissues but slightly, though it gives them a yellow tinge.

5. *Salt solution*.—Three-quarters per cent. solution of sodium chloride is practically a neutral solution; it alters the tissues but slightly, never causes any swelling, and is easily prepared by heating sodium chloride to redness, cooling it over sulphuric acid, and

dissolving 8 parts by weight in 1000 parts by measure of distilled water.

37. Tissues teased out and mounted in any of the above fluids retain an almost normal appearance and structure for a sufficient length of time to allow of careful examination, but little differentiation of structure is obtained. Snip off a fragment with a pair of curved scissors, put it on a clean glass slide *on a small* quantity of the neutral fluid (a single drop is usually quite sufficient). There should always be enough to allow of the tissue being bathed in the fluid, without air-bubbles being allowed to creep in, but never sufficient to *float* the cover-glass. With one of the needles fix the piece of tissue at one margin, and with the other tear off small fragments; these in turn are fixed with one needle, and torn with the other in the same manner, until they are small enough to be examined. Put on a cover-glass, and transfer to the stage of the microscope. In this operation a simple or dissecting microscope will prove of great assistance. This may be easily extemporised from the bull's-eye condenser by fitting a ring of blackened cardboard into the brass frame on the plane surface of the condenser. It is used as a simple lens, leaving it attached to the body of the microscope, or fastening it to an upright bar, say, of a retort stand. (The perforated cardboard, it will be understood, acts as a diaphragm.)

38. *Method of applying a cover-glass to these fresh preparations.*—Take a cover-glass by the edges between the forefinger and thumb of the left hand. Allow the edge to the left to come in contact with the left edge of the drop of mounting fluid. Then with a needle held *under* the right hand allow the right edge to descend slowly, taking care that the cover drives the fluid evenly before it and encloses no air-bubbles. If the cover is perfectly clean, the operation is readily enough performed; but if it is at all dirty, a considerable crop of air-bubbles is sure to result, in spite of the greatest care. Any air-bubbles in the mounting or examination medium should be carefully removed with the point of a needle before the cover-glass is applied.

39. Normal salt solution (§ 36 (5)) is also used in the process known as “pencilling.” A thin section of the tissue cut fresh and placed on

a glass slide is covered with the fluid, and then beaten with a camel-hair pencil. By this method the cells of a section of a lymphatic gland, for example, are set free from the network of delicate tissue in which they lie, and the different elements may be readily examined.

A similar or better result may be obtained by shaking the section in a test-tube containing a quantity of the salt solution.

40. Scrapings of fresh organs should also be examined. To obtain these, first squeeze out and wash away from the surface as much blood as possible, then carrying the knife at right angles to this surface, scrape off some of the juice, dilute it with neutral salt solution (§ 36 (5)), and examine at once. All fluids rich in cells may be treated in this fashion. Where the cells are not plentiful the fluid may be centrifugalised or may be allowed to stand in a conical glass; the sediment removed with a pipette may then be examined.

41. Lastly, thin sections of fresh tissues should always be examined both unstained and stained.

To make a section of most fresh tissues with an ordinary razor is a matter of some difficulty, and in its place a Valentin's knife may be used. This instrument is set to cut sections of a certain thickness between its two parallel blades; it is first *drawn by a single movement* through the organ of which a section is to be made, then suddenly turned, and a sharp cut is made at a considerable angle to the first, so as to separate the section. The blades are then unscrewed under water (it is best to use saline solution (§ 36 (5))) in which to manipulate the sections so made, and the section is transferred to a slide.

A more satisfactory plan of making fresh sections in the post-mortem room is by means of Cathcart's microtome (§ 87). A drop of gum placed on the plate is nearly frozen, and a thin slice of the tissue to be cut is placed on this, a little more gum is painted round the edges; the tissues are then frozen just hard enough to allow of their being cut easily; make sections and mount.

42. In the examination of fresh tissues it is sometimes necessary to alter, slightly, the refractive index of the protoplasm or of the contents of the cells, or it may be necessary to bring into greater prominence some one or other of these contents or the nucleus

by means of stains. For this purpose certain reagents may be used.

A 2·5 solution of acetic acid and a 2·0 solution of potassium hydrate are amongst the most useful for this purpose. In pus, for example, they clear up the protoplasm of the cell, thus allowing the nuclei, fat droplets, and bacteria to come into greater prominence. In using these reagents run them under the cover glass with the section or cells *in situ*, setting up a circulation of fluid by means of a piece of absorbent paper placed at the side of the cover glass away from the point at which the fluid is being added.

Stiles' nitric acid method for naked-eye examination of cancers.—Place thin slices of the fresh cancer (taken from the spreading margin) in a 5 per cent. watery solution of nitric acid for five minutes (they may be left for twelve hours). Then wash in water for five minutes or longer, when the connective tissue becomes gelatinous looking; from this the epithelial columns and masses stand out very prominently as opaque white streaks and points.

In place of a watery solution I have used 5 per cent. nitric acid in methylated spirit with equally good results.

Hydrochloric acid (5 per cent.) is used as a solvent for the carbonates of lime and magnesia, the dilute hydrochloric acid “replacing” the carbonic acid gas which is liberated in the form of small bubbles. (*Sulphuric acid* added gives rise to the formation of needle-shaped crystals of sulphate of lime.)

Lugol's solution (a mixture of iodine, potassium iodide, and distilled water in various proportions) is used for the detection of glycogen; it may also be used for staining fresh amyloid material. A good stock solution consists of—

Pure iodine	1 part.
Iodide of potassium	2 parts.
Water	40 „

This may be diluted with from $2\frac{1}{2}$ to $7\frac{1}{2}$ parts of water, the more dilute solution being most commonly used for microscopic work.

For bringing out the intercellular substance of epithelial cells, *e.g.*, of those lining the serous cavities, lymph spaces, and blood vessels, a 1 per cent. solution of nitrate of silver is valuable. The thin fragment of tissue to be examined is placed in this solution for a couple of minutes; as soon as the tissue becomes milky it is well washed in

distilled water and mounted in glycerin. The preparation is then exposed to the action of light; the outlines of the cells become marked by granular and blackened lines, the cell protoplasm remaining unaffected.

43. To mount these sections, float them in a large quantity of water or, better still, salt solution (§ 36 (5)), then taking the slide in the left hand, plunge it into the water in such a position that its under surface forms an angle of about 60° with the table: by moving the slide gently to and fro the section is brought from the bottom of the basin (if it has sunk); then, with the needle in the right hand, gently draw one edge of the section on to the slide, fix it there, and withdraw the slide from the water when the part of the section last in the water is floated out on to the slide. The slide is now turned round, and the margin which was first fixed may be floated out in the same way; and underlying or overlapping edges all round are similarly treated until the section is spread out, perfectly flat, on the glass slip.

Remember, in doing this, (1) to draw the margin a little beyond the centre of the slide when fixing the first edge, in order that the section may be near the centre; and (2) after fixing the edge with the needle, not to touch the section with the needle again, but to trust entirely to the movement in the water to spread out the crumpled edges. Apply a cover-glass (§ 38) and examine. A second section should be stained before it is mounted.

The best stains for these fresh specimens are picro-carmin (§ 102); methyl-violet (§ 117); fuchsin (§ 120); methylene-blue (§ 115); anilin blue black for nerve cells (Bevan Lewis) (§§ 128 and 129); and osmic acid (§ 135). Remember that alcohol causes great distortion of fresh tissues. In all cases, where possible, wash away the excess of stain with normal saline solution. Mount in glycerin (§ 194), Farrant's solution (§ 195), or Canada balsam (§ 199).

Fluids used for the purpose of macerating and isolating tissue elements without hardening them.

44. In some cases it is almost impossible to tease out fresh sections so as to obtain anything like satisfactory results. By macerating them in one of the following fluids, however, it is found that the tissue elements or cement substances may be so altered that the constituent parts are readily separated. In doing this it must be remembered that

the object is not to harden the tissues, but to isolate cells or fibres, and only a small quantity of the macerating fluid should be used for each fragment of tissue. The following are amongst the most useful :—

1. *Weak alcohol*.—1 part 96 per cent. spirit to 2 parts water (Ranvier). Macerate for twenty-four to forty-eight hours. This reagent is specially useful for the separation and examination of epithelial cells.

2. *Iodised serum* (§ 36 (4)) dissolves the intercellular cement substance in about thirty-six hours. It is also useful for macerating white nerve fibres.

3. *Common salt, 10 per cent. solution*, may be used to soften the cement substance of white fibrous tissue. It is useful in the study of fibromata, osteosarcomata, and similar growths.

4. *Caustic potash, 40 per cent. solution*, may be used for isolating the cells of non-striped muscle—*e.g.* myoma uteri. This seldom takes longer than from twenty minutes to an hour. Tease out, stain with picro-carmin (§ 102), and mount in Farrants's solution (§ 195). If time is available, and it is wished to obtain a permanent preparation of the muscle cells from such growths, use—

5. *Nitric acid, 20 per cent. solution*.—Soak small fragments of the muscular tissue in this fluid for twenty-four hours; wash well in water, tease, stain, and mount in glycerin. By this method the connective tissue is softened, and the muscle cells are hardened. A similar fluid for isolating nerve structures may be used—

Glycerin	1 part.
Water	3 parts.
Strong nitric acid	1 part.

Mix thoroughly. Place small fragments of the tissue in this fluid, leave for three or four days, and then wash well with distilled water.

6. *Ordinary Müller's fluid* (§ 62) may be used as a macerating fluid for nerve tissues, small pieces of which are left in a few drops of the medium for two or three days, and then teased out. They may then be examined in glycerin, water, or saline solution.

7. *Dilute chromic acid*, 0.1 to 1 per cent., may be used in the same way.

8. *Perosmic acid*, 1 per cent. Especially useful for defining the outlines of cells and for fatty tissues, which should be allowed to macerate

for from twelve to twenty-four hours before any attempt is made to tease them out.

9. *Acetic acid*, 1 per cent., for five or ten minutes, and then chromic acid, 1 per cent., for twenty-four or forty-eight hours. Stain in picrocarmine and examine in glycerin or in Farrants's solution (Arnold).

10. *Pure sulphuric acid* is recommended as a macerating fluid for the kidney and other glandular tissues. Wash thoroughly in plenty of water before examining.

These methods assume special importance in the study of the elements of which morbid growths are composed. For the various methods of artificial digestion, which are sometimes useful to the pathologist, the student is referred to special handbooks on histology.

45. It is often necessary to inject the vessels of an organ or of a tissue either to preserve the tissues or to distend the vessels of a tissue or organ before it is cut up or hardened. A good injection for the preservation of tissues is the following:—

Crystallised carbolic acid	1 part.	
Methylated spirit . . .	80 parts.	Dissolve and add
Pure glycerin . . .	80 „	

Mix very carefully and inject by pressure of head of fluid.

In making "distending" injections it is to be remembered that, in most cases, the patient has been dead for twenty-four hours before the inspection can be made, and that not only have the tissues undergone considerable structural changes, but they have also become considerably lowered in temperature. For these reasons, a gelatin injection fluid cannot be forced into the smaller ramifications of the blood vessels, unless certain precautions are taken to prevent the too rapid solidification of the gelatin. The tissues must be carefully heated throughout to 100° F. (38°·5 C.). In certain cases such elevation of temperature might give rise to considerable alterations in the tissues, especially where there is much epithelium, the cement substance of which has already become somewhat changed during the period that has elapsed after death; here it is necessary to use what may be spoken of as a *cold injection*, or one which is fluid at the ordinary temperature.

46. *Cold Injection Fluid.*

Soluble Prussian blue, which may be bought ready for use, is a very

convenient material with which to make a cold injecting fluid. Dissolve 2-5 parts of soluble Prussian blue in 100 parts of distilled water; add a few drops of hydrochloric or acetic acid before using.

After being injected, the organ should be plunged into weak methylated spirit (equal parts of spirit and water), to which a few drops of hydrochloric acid have been added; it is left in this for twenty-four hours, after which it may be cut up and the hardening process continued; or it may be hardened from the first in Müller's fluid (§ 62), or picric acid (§ 71). Sections should be washed in weak acid and mounted in camphor mounting fluid (§ 196), or in Canada balsam (§ 199).

Kollmann's cold carmine injection may also be used. It is prepared by dissolving 1 grm. of carmine in 15 drops of liq. ammoniæ and adding 20 c.c. of glycerin. This is added to a mixture of 1 grm. of common cooking salt dissolved in 30 c.c. glycerin; the whole is diluted with 50 c.c. of distilled water.

47. For capillary injections Cohnheim used a mixture of 1 part of anilin blue in 600 parts of 5 per cent. salt solution; and Hamilton recommends a $\frac{1}{4}$ per cent. watery solution of anilin blue-black, either alone or combined with 5 per cent. gelatin. These are both true solutions, and there are no particles, however fine, to become impacted in the minute blood vessels.

Rutherford mentions two injection masses used by Ludwig.

The first of these—asphalte, dissolved in chloroform and filtered,—is used for injecting the bile ducts. The special advantage of this fluid is “that chloroform, being an extremely mobile fluid, flows readily along the vessels, and that it readily evaporates and leaves them filled by a solid black mass.”

The second, “a solution of alcannin, in turpentine or in chloroform, was used by Ludwig for injecting lymphatics. The solution is of a bright red colour. Both the turpentine and the chloroform flow readily. When the latter is employed the chloroform evaporates, and leaves the alcannin in the vessels.”

48. Nitrate of silver cannot, as a rule, be employed by the pathologist as an injection fluid, as the tissues are dead before he can deal with them, and nitrate of silver does not act at all readily upon dead tissues. In the case of tumours, however, which may be obtained

whilst the tissues are still living, thin slices may be injected by absorption. Thin sections are placed in a $\frac{1}{2}$ per cent. solution of nitrate of silver (§ 137), where they are left for twelve hours. They are then transferred to a solution of equal parts of methylated spirit and glycerin. The sections should be mounted in glycerin.

49. The following injection masses are solid at ordinary temperatures, and can only be used in the case of animals newly killed or where the parts to be injected can be warmed to blood-heat.

Carmine Gelatin Injection Mass.

a. In a mortar pour 8 parts by measure of liq. ammoniæ on 4 parts by weight of carmine; an almost black paste will be formed if the carmine is pure; to this add 50 parts by measure of distilled water, and set the solution aside to filter.

b. In a tall glass jar, cover 10 parts by weight of pure gelatin (Cox and Coignet's) with distilled water; allow to stand until all the water is absorbed, and the gelatin is thoroughly softened.

Warm solution (*a*) in an earthenware jar or basin, placed in a pan of water (kept nearly boiling on a gas jet or near the fire), and add the gelatin; stir thoroughly, and, drop by drop, add a 10 per cent. solution of acetic acid until the alkalinity of the ammonia is neutralised.

The point at which this takes place will be recognised by the fact that the pungent odour of the ammonia is gradually lost, and that of acetic acid substituted, and also that a precipitation of the carmine takes place around the added acid, indicated by the fluid losing its bright carmine transparent colour and turning to a dull brownish-red. No precipitation should be seen when the fluid is examined under the microscope. In order to preserve this solution a small quantity of salicylic acid may be added. After injection keep the organ or tissue for twenty-four hours in equal parts of cooled spirit and water, to which has been added acetic or hydrochloric acid (1 part to 100). Continue hardening, as directed (§ 60), with spirit.

50. *Soluble Prussian Blue and Gelatin Injection Mass.*

Dissolve 5 parts by weight of soluble Prussian blue in 60 parts by measure of distilled water; add gelatin mass (*b* of § 49), warm, and add the salicylic acid. Harden the tissues as directed above.

In these injection masses the pigment is soluble in alkaline solutions, but is precipitated by acids; hence it cannot diffuse through the tissues,

whilst the gelatin still keeps it in a state of exceedingly fine division. This form of injection has the very great advantage over the fluid injections, that it keeps the vessels distended, as the gelatin is rapidly hardened by the action of the alcohol, and is not driven out when the injection tube is withdrawn on the following day.

51. A solution of gelatin prepared as above, but without the colouring material, is also an extremely good distending mass. It is perfectly clear, but takes on stains, especially carmine, very readily.

52. *Hoyer's Transparent Yellow Injection.*

(a) To two volumes of a cold saturated solution of bichromate of potash add one volume of gelatin solution containing 1 part of gelatin to 4 of water.

(b) To two volumes of cold saturated solution of sugar of lead add one volume of a similar gelatin solution; keep these separate.

When required for use heat (b) nearly to boiling-point and gradually pour in (a), stirring continuously. This injection is so fine that it will run into the lymphatics.

Injecting Apparatus

53. I. Cannulæ of different sizes are usually made of brass. The cannula should have a projecting rim near the nozzle, so that when tied it cannot slip out of the vessel; there should also be a cross bar, to which the threads may be fixed after being tied round the rim. This acts as a further preventive to the slipping out of the cannula.

For very small cannulæ, glass tubing drawn out and cut beyond the thinnest part, so as to leave a projecting rim, may be substituted for the brass. Notch the glass with a fine triangular file, and then round off the edges in a blow-pipe flame (Fig. 2).



FIG. 2.—Glass cannula with projecting rim.

II. (a) A brass syringe of at least 4 or 6 oz. capacity; for silver injections a glass or vulcanite syringe should be used.

or (b) A constant pressure apparatus.

III. A piece of brass tubing with a stop-cock.

All the cannulæ are made to fit one end of the brass tube (an

adapter of indiarubber tubing may be used for the glass cannulæ). The other end of the brass tube receives either the nozzle of the syringe or the tube from the constant pressure apparatus.

54. Select the nozzle which appears to be about the size of the vessel to be injected. Make an oblique incision into the vessel, and push in the cannula: pass a piece of thin but strong twine or thread around the vessel and the cannula, and tie firmly, drawing the tube back until the rim comes against the knot; make a second knot, and pass the two ends of the twine around the transverse bars on the tube, and make them fast. It is advisable in all cases to wash out the blood vessels with either cold or warm saline solution, according to the injection mass to be used. Into the open tube drop the injection, drop by drop, until all air is driven out, and put in the stop-cock tube with the tap open; fill it in the same way, and turn the tap off. Fill the syringe with the injection fluid; then turn the nozzle upwards, and drive the piston up gently, until all air-bubbles are expelled and only fluid comes. Open the stop-cock and allow the fluid to drop in as before; when the tube is filled, put in the nozzle of the syringe and slowly *rotate* the handle of the piston, and force home, gradually driving the injection into the vessels. *This cannot be done too slowly and steadily.* The syringe may have to be filled several times, and each time the same routine must be gone through, in order, as far as possible, to keep out air from the vessels.

55. In place of the syringe, the constant pressure apparatus may be used with advantage, as by it the pressure may be graduated with extreme nicety, and the injection may be made to run very slowly. Ludwig's mercury pressure apparatus, or some modification of it, is usually employed; but Stirling's water pressure apparatus is perhaps at once the cheapest, the most readily made, and quite as convenient as any. It is constructed as follows:—Fit a large wide-mouthed bottle and a smaller one with corks. In the larger cork bore four holes, and in the smaller one, two. Into two of the four holes in the larger cork fit two straight tubes, one passing nearly to the bottom of the bottle, the other passing for a distance of half an inch only through the cork. On this latter tube should be a stop-cock, and fitted above it a mercurial manometer by which the pressure is to be measured. This consists simply of a flattened U-shaped tube, one

bend of which is filled with mercury, fixed to an index board marked off in inches or centimetres. Into the other holes fit a couple of tubes

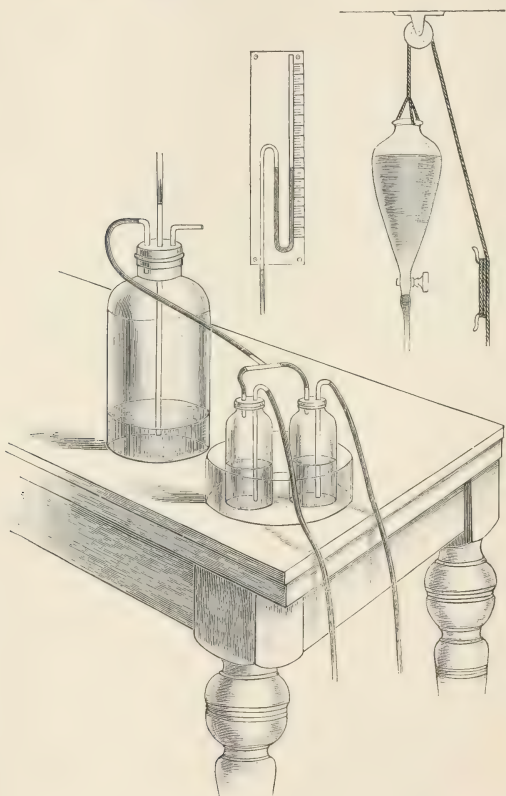


FIG. 3.—Constant pressure apparatus as described. The fourth tube, with stop-cock for allowing ingress and egress of air, is not represented in the diagram.

bent at right angles, each passing through the cork and projecting into the bottle for about half an inch, one of them having a stop-cock on the horizontal part of the tube. Into the two holes in the smaller

cork are fitted bent tubes, one of which passes to the bottom of the bottle, the other passing in for only half an inch. A tin or glass cylinder holding a couple of pints or more of water, or a Winchester quart bottle, fitted with the neck down into a large funnel, is suspended from a pulley fixed to the ceiling of the room by a cord, by means of which it can be raised or lowered at will. An indiarubber tube is carried from the bottom of the cylinder, or of the funnel, to the straight tube which passes to the bottom of the larger vessel. Instead of the above, pressure from a water main may be employed. From the open bent tube of the larger bottle a piece of flexible tubing is carried to the shorter bent tube in the smaller bottle, and attached to the longer bent tube in the smaller bottle is a flexible tube with a nozzle which will receive the stop-cock tube fitted into the cannula. The smaller bottle is filled with injection fluid, and both corks are driven well home. The stop-cock on the short tube bent at right angles (in the larger bottle) is closed, and the tin vessel or bottle is gradually raised; the water runs into the large bottle by the tube passing to the bottom; the air in this large bottle is thus gradually compressed, and is driven into the smaller bottle, and as the pressure on the surface of the injection fluid increases, it is driven out of the bottle and into the vessels which are to be filled. The pressure in the vessels is indicated on the manometer. This pressure is very readily regulated by merely raising or lowering the tin from which the water gets its "head," or by regulating the amount of water flowing from the main. The pressure should commence at half an inch of mercury, and be very gradually raised to 3 or 4 inches, according to the nature of the organ or tissue which is to be injected. In cases where it is necessary to make double injections, two, three, or even four small bottles containing different coloured injections may be used, but with care equally good results may be obtained with the above simple apparatus.

When the gelatin injection mass is used, the organ and the bottle containing the mass, and the syringe, must all be placed in a vessel of water, which should be maintained at a constant temperature of about (never above) 104° F. (40° C.) for an hour before the injection, and during the time that the injection is running.

A.B.—Always fill the tubes with the injection fluid before attaching to the cannula (the cannula having been already filled), in order that no air may get into the vessels.

METHODS OF FIXING AND HARDENING TISSUES

56. As already mentioned, it is an extremely difficult matter to obtain good permanent sections of fresh tissues, and even when sections have been obtained, the structural elements absorb water so freely that they do not remain sufficiently well defined. To get over these difficulties—*i.e.* to obtain thin sections, to obviate this absorption of water, and see the tissues in the natural state—it is found necessary to fix and then harden the tissue elements “as nearly as possible in their normal form and volume,” and especially to kill and fix the chromatin of the karyokinetic or mitotic figures of the nucleus. Indeed, it may be accepted that if these be well fixed, the cells are very slightly changed.

In the process of fixing and hardening, the protoplasm of the cells is toughened and rendered less liable to take up fluids. When working with normal tissues which have been removed from the body immediately after death, it is necessary to take the greatest care in carrying on the hardening process, but this care is even more necessary with pathological specimens that have been in the cadaver for at least twenty-four hours, and have therefore undergone considerable change, even in cold weather. For successful pathological investigation so much depends on this preliminary work, that the student is advised to pay attention to even the most minute details in connection with it.

GENERAL DIRECTIONS

57. *a.* Cut up the organ with a *sharp knife* or razor (taking care to make clean cuts, and not to drag or tear the tissue) into blocks about half an inch square and a quarter of an inch thick, or into cubes, each side of which should measure not more than about one-third to one-quarter of an inch. Where tissues are to be hardened rapidly, in absolute alcohol for example, such small thin blocks should always be prepared. These blocks should, in most cases, be taken from different parts of the organ or tissue to be examined, but one piece from the surface of an organ, with the capsule still attached, should always be included. In the case of the kidney, a triangular piece, including a portion of the cortex as the base of the wedge, and a medullary papilla as the apex, should be taken. Small portions from the different parts of a tumour—growing margin, centre, and intermediate area—should

always be selected. Hollow organs, such as stomach, bladder, or intestine, should first be slit open and then tacked down, with the mucous surface upwards, to pieces of board or cork. Delicate membranes, such as omentum, pia mater, etc., are best prepared by pinning them down to pieces of cork which have been moistened with the dilute hardening fluids. Large sections, half an inch thick, of whole organs should be laid in a flat-bottomed dish, or tied to wood or glass plates, with a layer of cotton wadding between the plate and the section, as may be found most convenient.

b. Put the tissues away in the hardening fluid *at once*.

c. Put a piece of rag or some cotton wadding, saturated with the hardening fluid, in the bottom of a wide-mouthed jar, on this place four or five of the blocks of tissue, then a second layer of rag or wadding, a second layer of tissue, and so on, *the proportion of tissue to fluid never being greater than 1 to 20*. Fill the jar with fluid, label distinctly with the name, age, and sex of the patient, the organ, the supposed morbid condition, and the date, time, and nature of the commencement of the hardening process. Keep in a cool dark place, an underground cellar being as good a place as can be used. Immediately before putting away, take the opportunity to change the position of the pieces of tissue in the bottle. This is especially necessary when spirit is used.

d. At the end of twenty-four hours pour out the fixing or hardening fluid, carefully wash out the jar, and rinse the tissue thoroughly with water to get rid of any blood or other deposit which may have settled, and which would, if left, seriously interfere with the hardening process; add fresh fluid.

e. Each time the fluid is changed the tissue should be carefully examined, and its consistency ascertained. When hardened properly, tissues should be tough and firm, never brittle, as they are apt to become, if the hardening process is carried too far or has been done imperfectly.

f. After being hardened slowly, the tissues are removed from the fluid, and if hardened in chromic salt solutions they are washed for several hours in water until no further yellow colour comes away; they are then transferred to a mixture of equal parts of methylated spirit and water for a couple of days, and then to methylated spirit, in which they are left until required. The spirit may become cloudy, in which case it must be changed, and again as often as any cloudiness appears.

g. It is an extremely difficult matter to give definite instructions as to the fluid to be used in individual cases, but the following general rules will materially assist in determining what hardening fluid should be employed. It should be noted that fewer fluids are now used than even a few years ago, some half-dozen fluids now sufficing for most laboratories.

- (1) Corrosive sublimate solution—saturated solution—7·5 per cent. (§ 61), alone or in combination with other reagents, is very valuable as a preliminary fixing reagent. It stops putrefactive processes and fixes the protoplasm at once. This, or Flemming's solution (§ 70), or one of the modifications of Flemming's fluid, is most valuable for perfectly fresh material.
- (2) Where a tissue is hard and firm, and not likely to shrivel on the abstraction of water, and where, too, it is not thought necessary to keep the blood in the organ, methylated spirit (§ 60) or absolute alcohol (§ 58) may be used. Tissues hardened in spirit are very readily stained with logwood or with the aniline dyes.
- (3) For very delicate tissues, or where there is much blood in the tissue to be hardened, or when it is very soft or œdematous, use Müller's fluid (§ 62) or Zenker's (§ 63) or Orth's (§ 64) modification thereof.
- (4) Osmic acid (§ 69) is an extremely useful fixing and hardening reagent for small objects of very delicate structure. It may also be used for hardening cancers, the salivary glands, small particles of tissue in which there is fatty degeneration, etc. Used along with chromic and acetic acids (§§ 70, 70a, and 70b) and with platinum salts it is an excellent fixative for preserving mitotic figures. Along with the chrome salts it is a valuable fixing and staining reagent for the tissues of the nerve centres.
- (5) If the presence of bacilli or bacteria is suspected, use absolute alcohol (§ 58). In some cases, however, a previous treatment with Müller's fluid (§ 62) will be found to have its advantages.
- (6) For the retina and for very delicate nerve tissues, a mixture of 3 parts Müller's fluid and 1 part of methylated spirit (§ 65), well cooled before it is used, is a very useful hardening reagent.

HARDENING FLUIDS

58. *Absolute alcohol* hardens tissues very rapidly. When preparing the intestines, stomach, and pancreas, dip the pieces into methylated spirit, and then place in a bottle in sufficient absolute alcohol to cover them; at the end of twenty-four hours again wash in methylated spirit, after which pour over them about twenty times their volume of alcohol. For tubercle, anthrax specimens, etc., plunge small pieces at once into a large quantity of absolute alcohol, and allow them to remain until thoroughly hardened, the process usually being complete in from three to ten days.

58a. *Victor Bonney's rapid method.*—Fix pieces of tissue not exceeding 9 c.mm. in diameter for five minutes in "acetic alcohol."

Absolute alcohol	2 parts.
Glacial acetic acid F.P. $14^{\circ}7-15^{\circ}$ C.	1 part.

Then transfer first to absolute alcohol in relatively large quantity for twenty-five minutes, changing the alcohol two or three times (dehydration is hastened by shaking the bottle), and then to xylol for ten or fifteen minutes, also in relatively large quantity; hasten the clearing by shaking. When the tissue is quite clear soak in melted paraffin for ten minutes, during which time the bath should be changed four times. Embed and cut sections (§ 94).

Coat a slide with egg-albumin mixture (§ 98), flood it with water and on this float the section. Warm the under surface of the slide by applying to it another slide previously heated in the Bunsen flame. Pour off the water and dry around the section, which is then pressed down to the slide with filter paper moistened with alcohol or methylated spirit; hold the slide over the Bunsen flame till the paraffin just melts; dip rapidly into two changes of xylol; afterwards remove the xylol by washing in two changes of pure methylated spirit; wash thoroughly in water and stain (§ 150).

59. A 10 per cent. solution of formalin in normal saline solution is an excellent fixative for many tissues. It possesses the very great advantage that it penetrates quickly and well, and fixes the tissues rapidly. Very thin pieces of tissue may be hardened in a couple of hours, whilst pieces one-third of an inch thick are

hardened in twenty-four hours. Although pieces can be left for an indefinite time in this formalin solution, it is well to continue the hardening process in the different dilutions of alcohol (§ 60). One of the great advantages of formalin fixation is that tissues can be frozen and cut in gum and syrup without any further preliminary treatment.

The vapour of 40 per cent. formol may be used as a fixative for blood films. The corpuscles are fixed at once (three to five seconds), and if the film be washed and hardened in absolute alcohol for one to twenty-four hours, excellent results are obtained (Scott).

60. *Methylated spirit* is used principally to complete the hardening process, but it may also be used as above for very firm tissues, especially where there is a large proportion of fresh epithelium, as in cancers, skin, etc. If used alone, as for waxy liver, it is changed at the end of twenty-four hours, and again at the end of a week. Tissues hardened in this way are ready for examination at the end of a fortnight. With most tissues hardened in spirit, it is well to put them away in equal parts of spirit and water, and only to put them into strong spirit at the end of twenty-four hours; or at this stage to add weak spirit again, and then at the end of forty-eight hours change into strong spirit. When changing the spirit it is specially necessary to wash away the precipitated blood, which will be found to have accumulated in considerable quantities on the specimens, and at the bottom of the bottle. This deposit, if left, interferes very much with the proper hardening of the specimens. Change the spirit at the end of the first week, and cut the tissue at the end of a fortnight. In combination with other fluids, methylated spirit is of very great value. In most cases tissues are first fixed with some other reagent; they are then transferred in turn to 50, 70, and 95 per cent. alcohol, and from this latter they are usually embedded.

61. *Corrosive sublimate (bichloride of mercury).*—Where tissues are moderately fresh, and often even where slight putrefactive changes have commenced, it is an exceedingly good plan to stop the putrefaction and to fix the elements of the tissue as far as possible by the use of bichloride of mercury before hardening them in spirit. Dissolve 7·5 grms. of bichloride of mercury in 100 c.c. of normal saline solution (0·7 per cent. common salt in water).

Or, better still, the following solution may be used, as it causes less shrinking :—

Bichloride of mercury	3 parts.
Glacial acetic acid	1 part.
Distilled water	100 parts.

In this, place portions of tissue about the size of a small bean, and allow them to remain for from six to twenty-four hours, then wash thoroughly in water, after which place them in a 30 per cent. solution of spirit to which a few drops of tincture of iodine have been added, the iodine serving to combine with and precipitate all the mercury that is left in the tissues, redissolve in weak iodide of potassium solution and wash thoroughly ; then place the pieces in 50, 75, and 90 per cent. spirit and absolute alcohol, each for twenty-four hours, after which the specimens may be embedded and cut.

62. *Chromic acid*, alone or in the form of some salt, is very frequently used as a hardening reagent. Of the combinations into which it enters, *Müller's fluid* is one of the most useful, especially in the preparation of delicate tissues, in which it fixes the protoplasm of the cells rather than hardens them, and thus causes but little shrinking ; for congested organs or mucoid tissues it is invaluable. To prepare it, take of

Potassium bichromate	2¼ parts.
Sodium sulphate	1 part.
Water	100 parts.

As in all other hardening methods, care should be taken to put in only one volume of tissue to twenty of fluid. Change the fluid at the end of the first, third, and seventh days, and then at the end of each week till the end of the fifth ; transfer to water for several hours, and then to dilute methylated spirit ; leave in this for from twenty-four to forty-eight hours, and then preserve in strong methylated spirit. The great advantages of Müller's fluid are, that there is no great danger of over-hardening, and although the process takes a considerable time, the results are almost invariably satisfactory ; the red blood corpuscles remain unchanged in shape and take on a greenish tinge ; and many tissues hardened in it, if not kept in too long, afterwards take on various stains more readily than when hardened in alcohol. It appears

that the sulphate of soda can penetrate almost any tissue, and where it once gets in the bichromate salt can follow. Consequently, it is not so essential that the pieces should be small, and this fluid may be used where it would be inconvenient to cut up the tissue into small cubes. Commence the hardening process as soon as the structures are taken from the body, and carry it on (except in the case of nerve tissues), for the first few days at any rate, in a cool dark place.

63. Perhaps the most generally useful modification of the above is Zenker's fluid. To ordinary Müller's fluid add 5 parts of corrosive sublimate, and keep this as a stock solution; then as the fluid is to be used, add 5 parts of acetic acid. In using this fluid the pieces of tissue should be thin and the fixing process should be carried out in about twenty-four hours; a longer or shorter time is required if the specimens are smaller or larger, but the pieces should never be larger than can be penetrated by the fluid in forty-eight hours. Even the most delicate structures are very perfectly preserved by this fluid. To continue the process of hardening and preservation wash thoroughly in a large quantity of water for twenty-four hours, and then carry through alcohol up to 80 per cent. (§ 61). To get rid of any mercury that may be precipitated, it is well before staining to place the *sections* in weak Lugol's solution for ten or fifteen minutes, and then wash them in alcohol. Zenker's fluid is now often used instead of Foa's solution, of which the following is the formula:—

(a) Saturated solution of corrosive sublimate in 0·8 per cent. physiological saline solution.

(b) Bichromate of potash 5 parts.

Water 100 „

Dissolve.

Take equal parts of *a* and *b*. Use *small* pieces of tissue, and treat as if it had been fixed in Zenker's fluid.

64. Orth recommends that to Müller's fluid in the quantities above given, 10 parts of commercial formalin should be added before the tissue is put away in it. It is well to use less rather than more formalin in making up this mixture; even small pieces of tissue may be hardened in three or four hours if the process be carried on in an

incubator. In any case tissues should not be left in this fluid for more than three days.

N.B.—Tissues should always be cut into *small* thin blocks where these hardening fluids are used. Wash in water for twenty-four hours and transfer to 80 per cent. alcohol.

64*a*. The ordinary fixing fluid used for Museum specimens serves also as a capital fixing fluid for material to be used for histological purposes—

Sodium sulphate	10 parts.
Magnesium sulphate	10 „
Sodium chloride	5 „
Dissolve in hot water	500 „
Add formalin	40 „

Leave in this fluid for from twelve to twenty-four hours; wash thoroughly in running water (otherwise the tissues become very brittle), and then treat as in § 60.

64*b*. *Beckton's modification of the Altmann-Schridde method of fixing and hardening tissues for the demonstration of granules and plasma cells.*

—In ordinary pathological work it is, as a rule, impossible to obtain a tissue absolutely fresh and warm. In certain cases, however, it may be taken from the freshly killed animal, or immediately after surgical operations. Cut the tissue into pieces 1 cm. in thickness, and place them in formol-Müller 1:49, kept at room temperature for one week, renewing the solution on the second and fourth days, and then in Müller's fluid (§ 62) for another week. Wash for twelve to twenty-four hours in running water, pass through alcohol of 25, 50, 75, 96 per cent. (§ 61), and three changes of 100 per cent. Embed in paraffin (§ 94), cut sections not thicker than 5 μ , fix on slides (§§ 98, 99).¹

65. *Müller's fluid and spirit* is recommended by Hamilton for hardening nerve tissues, brain, spinal cord, retina, intestinal muscle and glands. It is composed of

Müller's fluid	3 parts.
Methylated spirit	1 part.

¹ Schridde at this stage kept the sections in a 1 per cent. solution of osmic acid for one hour in the dark, then rinses them in distilled water and stains by the acid-fuchsin-picro method (§ 164). This osmic acid treatment appears, however, to be unnecessary.

Cool thoroughly before using, and follow the directions given for hardening with Müller's fluid.

66. For hardening brain tissue to be stained by Weigert's method, Erlicki's fluid may be used—

Potassium bichromate	2·5 parts.
Cupric sulphate	0·5 part.
Water	100 parts.

At the ordinary temperature this fluid hardens tissues in eight or ten days. At 40° C. tissues are hardened in four or five days. This method, however, gives rise to more shrinking of the tissues than does Müller's fluid.

67. Marchi's fluid used specially for fixing degenerated nerve tissues consists of

Müller's fluid	2 parts.
Osmic acid, 1 per cent.	1 part.

Fix in this for five or six days, then wash thoroughly in water and harden in alcohol.

68. *Nitric acid*.—For fresh tissues Brook recommends a preliminary fixation with 5–10 per cent. of nitric acid. (Altmann uses 3 per cent.) The method of procedure is as follows:—Place small pieces of tissue in the nitric acid solution for from one to two hours; wash thoroughly in 50 per cent. methylated spirit; change this two or three times to get rid of the acid, and then keep in 75 per cent. methylated spirit. Before cutting place the pieces for a day in 90 per cent. spirit, and then for an equal time in absolute alcohol.

None of the above hardening media give a permanent colour to the tissues; but the two following both harden and stain them.

69. *Osmic acid*.—As a hardening reagent osmic acid not only enters into the composition of the above fluids, but, alone, is extremely useful in the fixation of small pieces of delicate tissue, such as nerve fibres, retinal cells, and the like. It is used as a one-sixth to one-half or even a 1 per cent. solution. The tissue is allowed to remain in this, carefully protected from the light for about six, eight, or twenty-four

hours, according to its size and nature. From osmic acid transfer the tissue to 75 per cent. spirit, in which it may be kept until required; or after washing well in distilled water it may be placed at once in the gum and syrup solution, frozen, cut, and mounted in Farrants's solution, or, better still, in acetate of potash; glycerin being continually browned by the acid, unless the sections, before mounting, are thoroughly washed in water, or in water and glycerin. Osmic acid appears to tan the tissue, "fixing the tissue elements without producing a granular precipitate, or causing shrivelling" (Rutherford). Langley used osmic acid vapour for fixing the mucin granules in the cells of muciparous glands. This vapour is also valuable in the fixation of blood films.

Osmic acid enters into the composition of the following fixing solutions:—

70. Flemming's solution for fixing coccidia, nuclear figures in fresh tissues, tumours, scars, etc.—

Chromic acid, 1 per cent.	15 parts.
Osmic acid, 2 per cent.	4 „
Glacial acetic acid	1 part.

Always prepare fresh.

70a. Of the modifications of Flemming's solution Hermann's is said to give somewhat better results—

Osmic acid, 2 per cent.	4 parts.
Platinic chloride, 1 per cent.	15 „
Glacial acetic acid	1 part.

70b. Pianese's solution—

Chloride of platinum and sodium,		
1 per cent.	15 parts.
Chromic acid, 0.25 per cent.	5 „
Osmic acid, 2 per cent.,	5 „
Formic acid	1 drop to every 25 c.c.

Of any of these fluids use 10 to 20 parts to 1 of tissue. The pieces of tissue should not be more than $\frac{1}{12}$ of an inch thick. Allow to remain in the fluid for from one to three days; but tissues may remain for weeks, even exposed to sunlight, with no bad results. Wash thoroughly in water before cutting. After being fixed in this fluid,

tissues may be hardened by passing them through 30, 50, 75, and 90 per cent. spirit (one day each) and then into absolute alcohol; or they may be frozen and cut at once after they have been treated with 10 per cent. formalin. H. G. Plimmer recommends that sections fixed in fluids containing osmic acid should, when it is desired to bring out the nuclear figures, be bleached in hydrogen peroxide, and then—when bubbles have ceased forming—washed in distilled water. Nuclear stains then “take” well. Embed in paraffin (§ 94) or celloidin (§ 91).

71. *Picric acid, saturated solution*.—Fill a bottle with distilled water, add excess of crystals of picric acid, and simply fill up with water as the fluid is used, keeping crystals in the bottle to maintain saturation. Small pieces of tissue placed in this fluid should never be allowed to remain for more than from twenty-four to forty-eight hours; wash out the picric acid with 30 per cent. spirit, gradually raising the strength of the spirit to 75 per cent. In this way much of the swelling of the connective tissue elements is prevented. The great advantages of this method are that it hardens rapidly, and that tissues so hardened stain most beautifully with picro-carmin. It is specially useful for tumours and epithelial or epidermic structures, for the mesentery, and for small pieces of gland.

72. *Kleinenberg's picro-sulphuric acid*, for hardening soft sarcomata, myxomatous tissues, and embryonic tissues, is usually made as follows:—

Saturated watery solution of picric acid ,	. 100 parts.
Strong sulphuric acid	2 „

Filter to remove a yellow precipitate which is formed,
and add

Distilled water	300 „
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This will harden the above tissues in from three to twelve hours.

73. *Fixing by heat*.—For his work on the spleen, the late Professor Sanders used a method that is still employed for such organs or tissues as contain fluid albumin which it may be wished to coagulate *in situ*, as in cases of œdema of the lung, nephritis, etc. Small half-inch or

three-quarter inch cubes of such material are plunged into boiling water for from two to five minutes; they are then cooled rapidly in cold water, embedded in gum and syrup and frozen; or they may be hardened in spirit as above. Stain with alum carmine (§ 106), methylene-blue (§ 115), or hæmatein and van Gieson's fluid (§ 103).

74. Most tissues, when hardened in the above solutions, may be transferred to the gum and sugar solution, in which they may be kept perfectly well for an indefinite length of time, if sufficient carbolic acid is added to the mixture (§ 85); or they may be embedded in paraffin and kept in blocks ready for use (§ 94).

DECALCIFYING SOLUTIONS

are used for removing lime salts from bone and teeth, and at the same time hardening the organic matter.

75. *Picric acid, saturated solution*, made as above, takes some time (two or three weeks) to decalcify bone, unless the pieces are small, in which case maceration for eight or ten days may suffice; this solution is specially useful for softening young bones. Use a large quantity of the fluid, and add crystals from time to time; it is not necessary to change it at all until the bone is ready for cutting; when ready, wash out the picric acid and harden in 30 to 80 per cent. spirit.

76. *Chromic and nitric acid fluid* is made as follows:—Take of

Chromic acid	1 part.
Distilled water	200 parts.

Dissolve, and add

Strong nitric acid	2 „
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Put small pieces of bone into twenty times their volume of the fluid; change every third day until the end of the second week; wash well in water for twenty-four hours, and transfer first to weak, and then to strong, spirit (§ 62).

The best results are obtained by this method: the organic parts of the bone are hardened, whilst the nitric acid removes, very thoroughly, all calcareous material. Using these two methods no preliminary fixing and hardening are necessary.

77. *Nitric acid*.—Ten per cent. nitric acid may be used for decalcifying bone and fixing the softer tissues as above. Change the acid every day. A further or preliminary hardening with spirit (§ 60) is always necessary.

SIMPLE DECALCIFYING SOLUTIONS

The following decalcifying solutions and perhaps even nitric acid should be used only after the tissues have been hardened in alcohol (§ 58 or § 60), or one of the Müller's fluid group (§ 62), Zenker's (§ 63) and Orth (§ 64) fluids.

78. *Hydrochloric acid*, 10 per cent. solution. This removes the calcareous matter very thoroughly, but it must be remembered that it causes fibrous tissues to swell up. It is useful, however, for softening injected bone.

79. When it is wished to prevent the swelling of the softened fibrous tissue, *von Ebner's solution* may be used.

Common salt	2·5 parts.
Hydrochloric acid	2·5 „
Alcohol	500 „
Water	500 „

Use two or three hundred volumes of either of the above fluids to each volume of bone, and add sufficient acid, day by day, to thoroughly decalcify the bone. When this is done, the bone may be bent like a piece of indiarubber. It should then be thoroughly washed in water for a few hours, and transferred to a 10 per cent. salt solution until all acid reaction disappears (change the salt solution daily).

80. *Phloroglucin and nitric acid*.—Phloroglucin added to nitric acid is said by Mallory and Wright to protect the tissues, and so to allow of a stronger solution of the acid being used. It decalcifies very rapidly.

Phloroglucin	1 part.
Nitric acid	10 parts.

The fluid at first reddish-brown becomes light yellow in twenty-four hours.

Add nitric acid, 10 per cent. 100 parts.

The following formula is recommended as a solution acting more slowly :—

Phloroglucin	1 part.
Nitric acid	5 parts.
Alcohol	70 „
Water	30 „

81. *Paul Ziegler's sulphurous acid method.*—After the tissue has been fixed and hardened in formalin (§ 59) or Orth's fluid (§ 64), transfer at once to commercial sulphurous acid, and leave in this for from four to twenty-four hours according to the size of the piece of tissue. All decalcified material should be thoroughly washed with plenty of water and again hardened in 30–80 per cent. alcohol (§ 60).

METHODS OF CUTTING SECTIONS

82. Freezing, and other, microtomes are now to be obtained so cheaply that it is unnecessary for the student to waste time in learning to cut sections by hand. Various modifications of the freezing method have been suggested from time to time.

83. One of the great advantages of formalin (§ 59) as a fixative is that specimens fixed and hardened in it can be frozen at once after they have been rapidly washed in water, the freezing being done in water or gum as follows :—Take a piece of tissue not more than one-twelfth of an inch thick, rinse it in water, then placing a drop of water or gum on the plate of the freezing microtome, press the tissue down into position and as flat as possible on the freezing disc. Freeze and make sections at once. Remove the section from the knife with a camel's-hair brush, and transfer it to 60 per cent. alcohol in which all air-bubbles disappear. Wash thoroughly in water and stain.

84. Gaylord and Aschoff recommend that “if the section is very brittle it may be fixed to a slide or converted into a celloidin section in the following manner: from 60 per cent. alcohol the section is placed in absolute alcohol for three minutes. When free from water it is drawn out on a *perfectly clean* slide, pressed flat with a piece of

filter paper, and a solution of celloidin, prepared as follows, is poured over it :—

Photoxylin, celloidin, or gun cotton	. . .	10 parts.
Alcohol, absolute	100 „
Ether	500 „

Only sufficient celloidin to form a thin film is necessary, the remainder being allowed to flow back into the bottle.” The section should never be allowed to become dry. “When the celloidin begins to set, the slide is placed in a dish of water where the film may be stripped off with the aid of a needle, the celloidin being freed at the edges and raised carefully under the border; the detached celloidin film is trimmed into shape when it is ready for staining, or the section may be stained on the slide and detached later.” “The alcohol used should never be stronger than 93 per cent., and the section should be cleared with carbol-xylol or origanum oil and mounted in balsam.”

85. *D. J. Hamilton's method.*—Remove the hardening fluid from the tissue, especially if spirit has been used, by a prolonged immersion (say for twenty-four hours) in water, which should be constantly changed by allowing a very small stream from the tap to fall into the vessel in which the tissue is being washed. Then transfer to a mixture of (1) 4 parts of “gum acacia in *cold* water of the strength of 45·6 grms. of gum to 2400 c.c. of water. Saturate with boracic acid by boiling, and filter”; (2) 5 parts of “syrup of the strength of 28·5 grms. of pure sugar to 30 c.c. of water; while the syrup is boiling saturate it with boracic acid. Filter through muslin when cold”; and (3) 9 parts of water. For rather more delicate tissues one volume of syrup may be added to two volumes of the above mixture; whilst for such fragile structures as the retina, brain, or cord, a mixture of gum 5 parts and syrup 4 parts is recommended. Allow the tissue to remain in any of these mixtures for from twenty-four to forty-eight hours, or even longer. To each of these fluids add 3 drops per ounce of a strong solution of carbolic acid prepared by adding 1 part of Calvert's No. 4 carbolic acid to 2 parts of water, or saturate (boiling) with boracic acid, to prevent the formation of fungi. If this be attended to, the tissue may be left soaking in the solution for an indefinite length of time, and at the end will “cut” perfectly, if it has been properly hardened in the first

instance. The microtome is cooled down to such a point that a drop of gum (B.P. solution) placed on the die or disc (to be afterwards described) is frozen. The tissue which has been soaking in the gum and syrup is taken out with a pair of forceps, carefully dried in the folds of a soft cloth, put to soak for a few minutes in gum, and then adjusted as required on the surface of the cooled disc; gum is painted around it to keep it in position, and to form with it a solid firm mass, which may be cut. The mass is frozen just so hard that it will cut like a piece of cheese; when softer than this, it is not sufficiently frozen; when harder, it is very difficult to cut, especially if the sections are of considerable size.

86. Kuhne recommends that sections to be frozen should, after full dehydration, be transferred to oil of aniseed. Thin pieces are saturated and become clear in an hour. The tissue to be cut is then placed in the folds of a cloth to remove excess of oil, fixed on to the disc, frozen and cut in the ordinary way. The oil is removed by absolute alcohol, after which the sections may be stained and mounted by the usual methods.

THE FREEZING MICROTOME

87. Of this there are several very convenient forms, but it will be necessary here to mention a few only. Cathcart's ether microtome is ready for use at a moment's notice; from the student's point of view it has several very great advantages. It is portable, very clean to work with, its initial cost is moderate, and it can be very inexpensively worked.

The best instrument to use for making sections with this instrument is the blade of a carpenter's smoothing plane, used either with or without a wooden handle (recommended by Delépine). It works on two glass runners, so that the middle third of the blade comes in contact with nothing but the material to be cut, and consequently this portion remains sharp much longer than where there is simply a hole in the glass plate, as in some of the other microtomes. The elevating screw is worked with the left hand, and the knife with the right. In very hot weather it may be found necessary to stop cutting now and again, in order to use the spray and keep the tissue frozen; or the freezing apparatus may be handed over to an assistant. The screw

which raises the disc should be lubricated with glycerin, not with oil, which freezes too readily.¹

Instead of ether, carbonic acid gas compressed and stored in an iron cylinder may very conveniently be used.

88. Williams's ice-freezing microtome (made by Swift) is also an excellent instrument. With its aid, sections may be cut very rapidly with but little practice. The freezing box consists of a round wooden tub with an outlet pipe. The inner surface of the box is pitched or tarred to render it water-tight. In the centre of this is a stout brass pillar, screwed firmly down. On the upper surface of the pillar, dies of various sizes may be screwed for the reception of larger or smaller specimens. Covering the box is a lid, on which, embedded in pitch cement, is a plate of glass. In the centre of the lid is a round opening, through which the die is adjusted to the level of the upper surface of the glass. The cutting part of the apparatus consists of a razor, fitted into a triangular frame supported on three legs; each leg is a screw, one in front and two behind, and by raising or depressing these screws the distance of the triangle from the plate may be altered at will, and with the triangle, the razor. The edge of the razor is thus let down when the triangle is depressed in front, by simply turning the front screw out of the frame. (Thus, instead of bringing the tissue up to the razor, the edge of the razor is brought down to the tissue.) Fill the ice-box with salt and ice, layer upon layer; in summer this must be carefully attended to, but in winter the tissue will be frozen sufficiently hard if the box be but half filled. Fasten down the lid and screw in one of the dies. Pour on to the notched die a drop of gum solution, made by adding 1 part of gum to 2 parts of water. Remove the specimen to be cut from the gum and syrup solution or formalin, and place it on the drop of gum or water as soon as the first sign of freezing of the gum is seen at the margin. Hold it in the required position until it is firmly fixed. Then pour over the specimen sufficient gum to cover it completely, and freeze.

By means of the three screws bring the razor down to the level of

¹ This instrument, with all necessary apparatus (except the knife, for which an extra charge is made), may be obtained, price 17s. 6d., from A. Frazer, Teviot Place, Edinburgh. The planing-iron may be obtained for about a shilling from any tool warehouse.

the tissue, taking care to have all three legs equal in length. Grasp the tripod in the two hands, and with the forefinger give the large head of the screw at the apex of the triangle a turn through a very small angle, and push the frame, and with it the knife, obliquely forwards, keeping the three ivory-tipped legs resting firmly on the glass plate. A thin section will thus be made, the thickness of which is graduated by the angle through which the head of the front screw is turned. The thawing gum is quite sufficient to keep the knife moistened.

89. *Frazer's combination microtome*.—Frazer has succeeded in combining in a cheap and simple form the Williams and the Cathcart microtomes. His apparatus has the additional advantage that it may also be used for making sections of tissues embedded in paraffin.

For the more elaborate CO₂ freezing microtomes the student is referred to makers' catalogues.

90. Always remove the sections from the knife by means of a camel's-hair pencil; if the tissues are very delicate they must be transferred separately to a glass slide, where they are floated out and washed in 30 to 60 per cent. methylated spirit. With ordinary tissues, however, the sections are transferred at once to a basin of water, where they may be left from two to six hours (according to the temperature), after which the water should be changed and the sections left for a quarter of an hour, in order that the syrup and gum may be thoroughly washed out. If, then, it is found that air-bubbles are entangled in the sections, they should be well washed in methylated spirit and afterwards in water. They may be stained and examined at once; or if this should not be convenient, they may be kept in a mixture of equal parts of methylated spirit and glycerin, or in a fluid, made as follows:—Take of

Glycerin	15 parts.
Water	15 „
Carbolic acid, 1-20	1 part.

In place of this mixture methylated spirit may be used, especially if the sections are unstained.

For the method of cutting sections of whole organs, see Hamilton's "Pathology," and the author's paper in the *British Medical Journal*, 1888, vol. i. p. 737.

CELLOIDIN EMBEDDING

91. By the following methods tissues are kept in position, but it is not possible to obtain quite as thin sections as by the freezing method. Small thin sections of delicate tissues may be obtained of paraffin embedded specimens, but for large sections of the harder tissues the celloidin method is probably the more useful.

Thin pieces of tissue after being hardened are transferred to various grades of spirit (§ 60), then to absolute alcohol, and are placed for twenty-four hours in a mixture of equal parts of alcohol and ether. From this they are transferred to a very thin celloidin syrup (2 per cent.) made by dissolving Schering's granular celloidin in equal parts of ether and alcohol, where they are left from twenty-four to seventy-two hours, then to a stronger (4 per cent.), and, lastly, into a good thick syrup (6 per cent.) of the same material, allowing it to remain in each for twenty-four hours. Then take a piece of wood (not cork, which gives slightly in the jaws of the clamp) cut across the grain, and pour over the cross-grained surface a quantity of ether until no more bubbles make their appearance. (By several American workers vulcanised fibre is recommended in place of wood.) Over this prepared surface pour some of the thick celloidin, and embed the soaked tissues. Bank up well with the thick celloidin syrup, allowing it to dry for some time until there is a good firm film, add more celloidin, again dry, and then immerse in a large quantity of 85 per cent. methylated spirit until the whole is thoroughly hardened. It is possible to obtain sections as thin as $15\ \mu$ by this method, which may be used for embedding the spinal cord or brain tissue, and may also be utilised in making large sections of decalcified bone, skin, etc.

When it is necessary to leave the embedding material adhering to the section in order that the tissue may be kept in position, as in the case of the placenta, and where transparency is more important than thinness of section, photoxylin dissolved in equal parts of absolute alcohol and ether is sometimes recommended. Shrinkage is comparatively slight, and the embedding process is short and simple.

Tissues which have been passed through absolute alcohol are placed in $\frac{1}{2}$ -1 per cent. solution of photoxylin for twenty-four hours; they are then transferred to a 5 per cent. solution of the same material, and left there for from thirty to forty-eight hours. If the fluids be kept warm, the infiltration of the tissues goes on more rapidly. The tissue

is then luted on to a piece of wood as above, and left in 70 per cent. alcohol for three hours. Clear with origanum oil (§ 193) and mount in xylol balsam (§ 199).

92. Celloidin embedded specimens are best cut under spirit, and to carry out this I have devised the following modification of the Schanze microtome:—To the knife-block that runs in the groove is fixed a second bevelled plate, so adjusted that it throws down the point of the knife about 2 inches. This bevelled block is sufficiently long to carry both the knife and the steadying clamp that runs to the end of the blade. It will be evident that the knife will not run parallel to the ground, but at an angle. To the body of the microtome is fixed, by movable clamps, a nickelled copper tray, only about a quarter of an inch deep where it is attached, but $2\frac{1}{4}$ inches deep at its outer part. In the bottom of the tray is a rounded opening, $5\frac{1}{2}$ inches in diameter, through which the specimen clamp passes. The space between the margin of the opening and the rod supporting the clamp is filled in by an indiarubber bag (Nachet's plan), fixed by a wire to a flange around the opening, and, by a nut with a washer, around the clamp-supporting rod. The tray is filled with spirit, which cannot escape except by special taps, but the specimen can be raised by means of the screw, the indiarubber bag allowing considerable movement but preventing the escape of the spirit. At one corner of the tray is a grating with a tap beneath by which the spirit may be drawn off, whilst in the indiarubber bag is fitted a tube provided with a Mohr's clip, through which the remainder of the spirit may be removed. At each end of the body of the microtome is a collar with a binding screw, in which a rod may be fixed to prevent the knife point or heel from coming in contact with the ends of the tray. For large sections this apparatus is very useful indeed. It was made for me by Hume, Edinburgh; it may also be obtained from A. H. Baird, Edinburgh.

93. *Serial sections (celloidin).*—For mounting serial sections of specimens cut in either celloidin or paraffin I now use Al. Obregia's modification of Weigert's method. (1) Make a solution of sugar candy in water, about as thick as ordinary syrup. To 30 c.c. of this add 20 c.c. of 90 per cent. alcohol and 10 c.c. of a solution of pure dextrin of the consistence of syrup. Spread a thin layer of this over a slide and

allow it to dry in a warm place, a thermostat, protecting it from dust ; keep for several days.

(2) Dissolve photoxylin, celloidin, or gun cotton, 6 grms., in a mixture of absolute alcohol, 100 c.c., ether (pure), 300 c.c. ; allow it to stand, and pour off the clear part. Both this and No. 1 should be preserved in stoppered bottles. Cut pieces of satin cooking paper (which is thin and leaves no particles on the sections) the size of the slides, place in a flat dish with the smooth surface upwards, and moisten with 95 per cent. alcohol. Remove the sections with similar paper, and arrange on the slips in the dish, spreading them well out with a camel's-hair pencil moistened in alcohol. Then remove the paper and lay it, with the sections upwards, on folded blotting paper until all fluid is absorbed, then place the paper, face downwards, on a prepared slide, so that the sections come in contact with the dextrin ; place blotting paper over it, press lightly with the finger, and remove the paper, leaving the sections on the prepared layer. Then pour over the slide solution No. 2 and wave in the air until all cloudiness disappears. Number with iron ink. Put the slide into pure water, which dissolves off the sugar, when the whole film comes easily away from the glass, leaving one side quite uncovered, so that all processes of staining, washing, and dehydrating may go on more quickly than when both surfaces are covered with a collodion film. For brain sections this is an exceedingly satisfactory method, as the medium is not stained by either carmine or hæmatoxylin, although it is stained by aniline colours ; these, however, may be removed by strong acids.

SERIAL SECTIONS (PARAFFIN)

94. Paraffin embedding has been so perfected that much time may often be saved by using paraffin when it is essential to obtain serial or specially thin sections. Indeed this is now a routine method. Small pieces of tissue that have been well hardened and then soaked for six to twenty-four hours in absolute alcohol, are immersed in *clean*, pure turpentine, xylol, or chloroform, placed in a covered porcelain crucible. This is put into a warm chamber, where it is gradually heated up to the melting-point of the paraffin that is used, and left for from three to twenty-four hours until the tissue is transparent. It is then transferred directly to a hard paraffin which melts at 53° C. (very delicate objects should be passed through several softer paraffins

—melting at 45° to 50° C. or through a saturated solution of paraffin in one of the above solvents), the tissue is allowed to soak in the paraffin solution and then in pure paraffin for several hours, and is then transferred to a paper boat, pill-box, or metal mould full of melted paraffin. It is kept in position with warm needles, and is cooled rapidly by floating the boat in water. There should be none of the paraffin solvent left in the tissue or in the paraffin. When the specimens are to be stained in bulk they should be taken from 75 per cent. spirit, stained, and then passed in turn through 90 per cent. spirit and absolute alcohol, after which they are treated as above.

These paraffin blocks are best fitted to movable dies. Fix the die in a large cork, warm in a Bunsen flame, then carefully heat the under surface of the paraffin block and press it firmly down on to the die, which should forthwith be plunged into cold water, this at once causing setting of the paraffin between the die and the block. Pare the block down to a rectangular form, two sides being quite parallel; the two other sides (ends) being pared as close to the tissue as possible.

METHODS FOR PRESERVING AND MOUNTING DELICATE TISSUES AND STRUCTURES

95. *Combined photoxylin and paraffin method.*—For certain delicate tissues Richard Muir recommends the following:—Harden the tissues (§ 57) and soak for twelve hours each, first in absolute alcohol and then in a mixture of equal parts of absolute alcohol and ether, transfer to a moderately thick solution of photoxylin for twenty-four hours, and then to oil of origanum and equal parts of this oil and paraffin for twelve hours. This latter mixture should be maintained at a temperature never rising above 40° C., and therefore should be kept on the top of the paraffin oven, *not inside*. Embed in pure paraffin (§ 94) and cut as usual.

Where bones are to be embedded softer paraffin should be used, and where Webster's method of cutting large sections in paraffin (*Laboratory Reports*, R.C.P.Ed., 1891, vol. iii. p. 266) is used, it is always better to embed in the softer mass.

96. Any of the microtomes already mentioned may be used for cutting these paraffin sections. The one that I now use is the

rocking microtome of the Cambridge Scientific Instrument Company, which—with dies instead of a hollow tube, and some other improvements suggested by G. Brook and myself, and carried out by Frazer of Edinburgh—is a capital instrument. Minot's "precision" microtome, made by Bausch and Lomb, and the Minot-Blake microtome, are also excellent. The German and French makers also turn out very good instruments, but they seem to me to have no special advantages over the above, of which it is not necessary to give a description, as full directions for its use are sent out with each instrument.

97. Kuhne's rapid aniseed oil method may be applied to tissues to be embedded in paraffin. Saturate a small piece of tissue with aniseed oil (§ 86). Remove excess of oil with a clean cloth or filter paper and plunge at once into a bath of melted paraffin. Complete the embedding process *secundum artem*.

98. *Fixing serial sections on the slide where paraffin is used* as the embedding medium. When sections are very friable, or when serial sections are to be made, it is well to fix them to the slide by one of the following methods:—

Mayer's method.—Take of filtered white of egg (well beaten up and then filtered) and glycerin, equal parts; mix thoroughly, and add a crystal of thymol, or salicylic acid, or some scraps of camphor. On the slide, or, better still, the cover glass, in the position in which the sections are to be fixed, spread a layer of this mixture, wiping off *all excess* with a soft clean cloth so as to leave as thin and equable a layer as possible. Float out the sections on warm water (10° lower than the melting-point of the paraffin used), float them to the desired position on this film of albumin, drain off the water, and heat the slide or cover glass over a Bunsen flame until the albumin is fixed or coagulated and the paraffin melted. Wash away the melted paraffin with *warm* turpentine or with xylol, pouring on several relays of the fluid until the whole of the paraffin is removed. Then immerse the glass, with the adherent sections, first in methylated spirit, then in turpentine or clove oil (§ 193), to get rid of the granularity of the albumin, and mount in Canada balsam (§ 199). If the sections have not already been stained "in bulk," they may be easily stained with any of the ordinary stains after the paraffin has been dissolved out

by the xylol and they have been washed in spirit. The sections are afterwards thoroughly dehydrated with absolute alcohol, cleared up in xylol, and mounted in balsam (§ 199); picro-carmin stained specimens should be mounted in Farrants's solution (§ 195). Instead of using albumin and glycerin, the sections may be arranged by means of a camel's-hair pencil moistened with alcohol on a slide moistened with alcohol. The slide is then warmed when the sections adhere moderately firmly, and on raising the temperature still higher the paraffin may be melted, after which it may be dissolved off by means of xylol or turpentine. The sections are then rinsed with alcohol if they are to be stained on the slide, after which the method of procedure is as above.

99. *Gulland* recommends the following method, and with it excellent results may be obtained, especially where it is wished to obtain clean well-differentiated sections. Allow one end of the ribbon of paraffin sections or a single section to float out on warm water. (I find that 8° or 10° C. below the melting-point of the hard paraffin used gives the best results.) Then float and arrange on a clean slide (or cover glass), tilt the glass on one edge and allow all superfluous water to drain away. Then place the sections as they lie on the glass on the top of a copper oven, maintained at a temperature 2° or 3° C. above the melting-point of the paraffin, the temperature on the top outside then being 2° or 3° C. below the melting-point, and allow them to remain until all moisture has evaporated. Cover the sections with cardboard to protect them from dust. When all moisture has evaporated, the sections become clear and now adhere firmly to the glass. Then place them inside the oven for a little until the paraffin melts and wash with turpentine or xylol. The drying process takes from one to six hours, but the sections may be left still longer with advantage and with no harm to the tissue, so long as the paraffin is not allowed to melt until the fixation is complete and you are ready to carry out the staining and mounting.

100. Schällibaum's collodion fixing method may be used where the sections have been stained in bulk. A mixture of 1 part collodion and 3 parts of clove or lavender oil is spread in a very thin layer on a slide with a glass rod or the edge of a glass slide, the sections are placed in position on the slide and then warmed over a water bath or

naked flame until the oil is evaporated; the sections are then washed with xylol or turpentine to get rid of the paraffin, and are mounted in benzol or xylol balsam (§ 199).

Using Al. Obregia's method for sections cut in paraffin, they are arranged on the surface of the dried syrup with a camel's-hair pencil, flattened out and heated in a warm chamber kept at 57° to 60° C. for ten minutes, when the sections have a tendency to become more perfectly spread out. The paraffin is first removed with good blotting paper, then with xylol or turpentine, after which the slide is placed in absolute alcohol for a few minutes, and quickly into photoxylin solution; dry for ten minutes, then wash in water and stain. To dehydrate afterwards use 95 per cent. spirit, and to clear use pure carbohc acid crystals, 1 part, to xylol (pure), 3 parts.¹

METHODS OF STAINING SECTIONS

101. In all cases sections should first be examined unstained, and again after they have been acted upon by various special reagents. Whatever may be the nature of the reagent employed, it is used for the purpose of bringing into greater prominence special structures, or to differentiate one structure from the others in which it lies. Thus it has been found that the nuclei of cells are more deeply stained by most staining reagents (carmine, etc.) than are the surrounding parts; that a few reagents, such as picric acid, have a special affinity for the formed material of the cell; that the cement substance between cells may be specially picked out, as by nitrate of silver; or, that certain parts may become "cleared up," so that other structures may be seen more distinctly.

In the following directions given for staining tissues, special prominence will be accorded to such methods as are found to be most useful to the pathological histologist, which methods, none of them very complicated, usually give most satisfactory results.

102. *Picro-carmine*.—Though it is now somewhat neglected by the histologist, one of the most useful staining reagents is Ranvier's picro-carmine staining fluid or picro-carminate of ammonia. When the fluid is properly prepared and the staining process is well carried out, the most brilliant double-staining effects are obtained.

¹ See also Gulland's modification, *Journ. Path. and Bact.*, Edin., 1893, vol. i. p. 391.

It is prepared as follows :—Take of

Pure carmine	1 part.
Liq. ammoniæ	3 parts.
Distilled water	3 „

Dissolve the carmine in a test-tube with the ammonia and water. To this add 200 parts of a cold, saturated, and filtered solution of picric acid, and mix thoroughly. Place the fluid in a basin and cover with a clock glass (with the concave surface upwards to keep out dust, and to allow of the moisture falling back into the basin, so that the exposure to the sunlight may be prolonged), and allow it to evaporate in *strong sunlight*, testing it every few days by staining a section of skin, until the nuclei and fibrous tissue are stained distinctly pink, and the epithelial cells, especially those of the horny layer, are stained yellow. The best double-staining is usually given before the fluid has evaporated down to half its bulk, and at this stage it is sometimes found that crystals of picric acid are deposited in the tissues. To obviate this, it is necessary to add 10 or 20 per cent. of distilled water to the fluid that remains. To prevent the growth of fungi add from 2 to 6 drops of 1–20 carbolic acid solution to each ounce of the fluid; filter, and keep in a glass-stoppered bottle. Some workers use the fluid without any evaporation at all, and appear to obtain fairly satisfactory results.

To stain a section, spread it out flat on the glass slip (§ 43), drain off the superfluous water, and run several drops of the staining fluid (not diluted) over it; allow it to stand for from three to five minutes exposed to sunlight, covered with a watch-glass to keep off the dust. (In winter it is well to warm gently over a spirit lamp, the slide on which the section is being stained, as slight heat causes the tissues to stain both more rapidly and more brilliantly.)

Do not wash the section, but simply run off the superfluous fluid by tilting the slide, and then wipe round the section with the thumb, or with a soft clean cloth; be careful not to remove the whole of the staining fluid, as any slight excess is gradually taken up by the tissues after the section has been mounted either in Farrant's solution (§ 195) or in glycerin (§ 194), to which from 1 to 5 per cent. of formic acid has been added. The full effects of the stain are not seen at once, but after the section has been mounted for two or three days,

especially if a small quantity of the staining fluid has been left on the section, and if the slide has been kept in a warm place, a beautiful selective double-stain is obtained. The nuclei of cells and fibrous tissue are stained brilliant crimson or pink, whilst the formed material of epithelial cells, elastic tissue, and dead material are stained yellow. Thus, in a section of the skin, the horny layer, the stratum Malpighii, hairs and muscles, are stained various shades of yellow, whilst the nuclei of the cells in the deeper layers of the epidermis are stained crimson, as also is the tissue of the cutis vera. In a section of a scirrhus cancer the stroma assumes a delicate pink, the indifferent tissue, which is made up of rapidly proliferating connective tissue corpuscles and leucocytes, takes on a rich crimson colour, whilst the cancer cells are stained yellow or brown, the nuclei appearing of the same tint as the cells of the indifferent tissue.

In a tubercle "follicle" the double-staining also comes out very well. The centre of the giant cell takes on a canary yellow colour; surrounding this is usually a zone of nuclei stained brilliant orange-red, and outside this again is the reticulum with the endothelioid cells stained crimson; the condensed fibrous-looking capsule at the periphery being stained pink, and the small round cells much the same as in the indifferent tissue of the scirrhus cancer. When caseation has commenced in the centre, the yellow mass assumes a somewhat granular appearance and loses its brightness. When it is wished to mount the section in Canada balsam, special precautions have to be taken to retain the picric acid stain. Stain the section for a longer time, as much as an hour being sometimes necessary; then wash in glycerin to which 1 per cent. of hydrochloric acid has been added, and that has been tinged with picric acid; dehydrate with alcohol, also coloured with picric acid, clear in clove oil (§ 193), and mount in balsam (§ 199). For some purposes this gives very good results, but it is not so generally useful as is Farrants's method (§ 195).

103. *Van Gieson's method.*—Although an excellent stain when properly prepared and used, Ranvier's picro-carmin is certainly not easily or consistently prepared, and the hæmatein and van Gieson stain has now largely taken its place, as the results obtained with it are, on the average, better than those obtained by the picro-carmin method.

Prepare (a) Mayer's alum hæmatein—

Hæmatein	1 part.
Alcohol, 90 per cent.	50 parts.
Alum	50 „

Dissolve the hæmatein in the alcohol, placing the mixture in an incubator. Then dissolve the alum in 1000 parts of water and mix the two solutions. Before using, filter and dilute the solution with weak alum solution. The addition of 2 per cent. of glacial acetic acid to the above stain renders it a better nuclear stain.

Even better than the above for this purpose is Weigert's iron hæmatoxylin (§ 110 (b)).

(b) Van Gieson's picro-fuchsin stain—

Saturated aqueous solution of picric acid	100 parts.
Saturated aqueous solution of acid fuchsin, added until a deep red colour is obtained, usually	1 to 3 „

Mix and filter.

Stain the section for from ten to twenty minutes or more in the hæmatein solution, wash thoroughly in tap water until the section takes on a good blue tinge. Transfer to van Gieson's stain and leave for a few seconds. Wash very rapidly (a) in water and (b) in 96 per cent. spirit. Remember that the fuchsin is removed by water, the picric acid by alcohol. Clear in a mixture of

Beechwood creosote	1 part.
Turpentine	4 parts.

Then for a couple of minutes in xylol (§ 193) ; mount in Canada balsam (§ 199). This stain may be used to bring the axis cylinders of nerves into prominence.

104. Specimens stained by this method do not retain the initial vivid contrasts for any great length of time, and sections so stained for immediate examination should be stained in duplicate by Powell White's hæmatein and erythrosin method, as modified by my laboratory superintendent, E. E. Stubbings. Here the van Gieson stain is replaced by the following :

Grübler's erythrosin, saturated alcoholic solu- tion	20 parts
Picric acid, saturated watery solution	90 „

Add precipitated calcium carbonate in excess.

Allow to stand for some time, shaking up at intervals, and filter before use.

After staining in hæmatein, as in van Gieson's method, differentiating with dilute acetic or hydrochloric acid and washing thoroughly in water, stain in the above fluid for from one to ten minutes; wash rapidly in spirit and then in absolute alcohol; clear in the creosote and turpentine mixture (§ 103), then in xylol (§ 193), and mount in Canada balsam (§ 199). This does not give quite such good immediate results as the van Gieson method, but the nuclei do not decolorise, and the stain is permanent.

105. *Carmine staining fluid* is especially useful for sections of the central nervous system, and for structures in which are considerable quantities of fibrous tissue. As a staining reagent for most tissues, it has been superseded by the stains already described. To prepare it, take of

Pure carmine	1 part.
Liq. ammoniæ	1 „
Water	50 parts.

Triturate the carmine in a mortar, add sufficient water to form a paste, and then add the ammonia, when the paste will at once turn from a bright red to almost black if the carmine is pure. Add the rest of the water, and keep the solution in a glass-stoppered bottle in which is suspended a piece of camphor. It is sometimes recommended that double or treble the quantity of ammonia be added, and then allowed to evaporate until no ammoniacal odour remains.

After carefully washing out picric acid or any of the chromates, a section may be stained rapidly by spreading it out on the glass slide, (§ 43), and running a drop or two of the solution over it; allow it to stand for from three to five minutes, and then wash in water for a couple of seconds, and transfer rapidly to acidulated water (8 drops of acetic acid to a pint basinful of water). This last part of the operation must never be neglected, as the carmine is held in solution by an alkaline fluid, and is only precipitated in the tissues when the fluid is rendered acid. Where the stain is properly selective, the nuclei and fully formed fibrous tissue are stained carmine and a delicate pink respectively; other formed material remains unstained, or is only slightly tinted. The axis cylinders of medullated nerve fibres are

stained brilliant carmine, as are also the nerve cells of the cord, etc., the latter not so deeply. A more selective stain is obtained by staining the sections slowly in a watery solution. The sections are afterwards washed in water slightly acidulated with acetic acid, mounted in glycerin (§ 194) or Farrant's solution (§ 195). When it is wished to clear up the section still further, it may be mounted in Canada balsam (§ 199).

106. *Alum carmine* sometimes gives very good results, but it may be a somewhat disappointing stain. Method of preparation—

Carmine (pure)	2 parts.
Alum	5 „
Water	100 „

Boil for an hour, allow to cool, and filter. Add a crystal or two of thymol.

Sections may be left in this for ten minutes or twenty-four hours, as they never over-stain; wash thoroughly in water and mount in balsam.

107. Orth's lithium carmine is sometimes used as a contrast stain for tissues containing bacteria stained with anilin dyes. It is prepared as follows:—

Carmine	5 parts.
Saturated aqueous solution of lithium carbonate	100	„
Thymol—a few crystals.		

Dissolve in the cold: *always filter this solution before using it.*

108. As already mentioned, hæmatoxylin or hæmatein (which is the real stain in the logwood) has to a large extent ousted carmine as a nuclear stain. It has the special advantage that it may be made to stain the protoplasm of cells slightly and even the fibrillar elements in the tissues. All the preparations made up from hæmatoxylin require time to ripen by oxidation, hæmatein being formed in this process. The hæmatein combining with alum forms a bluish solution which, according to Mallory and Wright, "is precipitated in the tissues (chiefly in the nuclei) by certain organic and inorganic salts there present, as, for instance, phosphates." They also draw attention to the fact that "Mayer and Unna have shown that it is possible to oxidise and to ripen in an instant a solution of alum and hæmatoxylin by adding to it a little peroxide of hydrogen neutralised by a crystal of

soda." In preparing any of the hæmatoxylin or hæmatein solutions, the alum should be quite iron-free, and should be as fresh as possible. In most of the hæmatein and hæmatoxylin solutions, owing to continued oxidation of the hæmatein after the fluid has thoroughly ripened, a precipitate may be formed. This should always be filtered off just before the stain is used, and it is well to add a little fresh alum from time to time if it is desired to obtain a good nuclear stain, and especially when sections are cut in celloidin, the diffuse stain attacking celloidin, the nuclear stain leaving it unaffected.

109. Out of the numerous formulæ given by various authors the following are perhaps the best :—

(a) Mayer's alum hæmatein (§ 103 (a)).

(b) Extract of hæmatoxylin	3 parts.
Ammonia alum	1 part.
Glycerin	200 parts.
Water	400 „

Mix the extract of hæmatoxylin, alum, and water, and allow to stand for four days, shaking well three or four times a day, add the glycerin and boil down to $\frac{5}{6}$ of the original bulk, throwing in 2 or 3 grains of alum, whereupon the colour becomes much more brilliant, and add a crystal of thymol dissolved in alcohol in order to preserve the fluid. The glycerin in this and the following solutions appears to act as a preservative to the hæmatein alum combination, preventing its further oxidation.

(c) An excellent formula for hæmatoxylin is that suggested by Delafield—

Hæmatoxylin crystals	4 parts.
Alcohol, 95 per cent.	25 „
Saturated aqueous solution of ammonia alum		400 „

Dissolve the hæmatoxylin in the alcohol, add the alum solution, and expose the mixture in a wide-mouthed vessel to light and air for three or four days. Filter and add

Glycerin	100 parts.
Alcohol, 95 per cent.	100 „

Again expose to light until the fluid assumes a deep purplish colour. Then filter and store in a well-stoppered bottle,

110. Iron alum hæmatoxylin stains—

(α) Heidenhain's formula —

(α) 2·5 per cent. solution of iron alum sulphate or iron ammonium sulphate.

(β) Hæmatoxylin	1 part.
Absolute alcohol	10 parts.
Water	90 „

Ripen for at least one month.

Place the section in solution (α) and leave for six to twelve hours. Wash in water and transfer to (β) for twenty-four hours. Wash in water and differentiate in (α), watching the process under a low power lens until nuclear structures stand out sharply. Wash in running water for fifteen minutes, dehydrate in alcohol, clear in oil of cloves (§ 193), and mount in Canada balsam (§ 199); see also § 139.

(β) In Weigert's iron hæmatoxylin the iron is contained in the staining solution; no previous mordanting is necessary.

Solution (1) Hæmatoxylin	1 grm.
Alcohol (96 per cent.)	100 c.c.
Solution (2) Liq. ferri perchloridi (30 per cent.)	4 „
Hydrochloric acid conc.	1 „
Water	100 „

Both solutions keep well; the first must be allowed to ripen, but at the end of six months it stains rather diffusely, possibly from over-oxidisation. Just before the stain is to be used, mix equal parts of each solution. This mixture should be used at once; it does not give the best effects after five or six days. Differentiation in acid alcohol is not necessary (Weigert), although sometimes advisable. This is preferable to Mayer's hæmatein as a nuclear stain in the van Gieson method. The stain is not so stable as is the alum hæmatein and does not keep so well, but it stains much more rapidly and satisfactorily.

111. Boehmer's hæmatoxylin—

(α) Hæmatoxylin crystals	1 part.
Absolute alcohol	10 parts.

Dissolve.

(β) Ammonia alum	20 parts.
Distilled water, boiling	200 „

Cool and filter. At the end of twenty-four hours mix α and β , exposing the mixture to the air and light for eight days in an open wide-mouthed vessel, filter and store in a well-stoppered bottle.

112. For many kinds of work Ehrlich's acid hæmatoxylin is to be recommended, especially as a groundwork for double and triple staining. Dissolve hæmatoxylin, 2 parts, in 60 parts absolute alcohol. To this add 60 parts of glycerin and 60 parts of water, both of which are previously saturated with alum, and 3 parts of glacial acetic acid. The great advantage of this solution is that it does not cause over-staining nearly so readily as do some of the other hæmatoxylin preparations. It should be kept exposed to the light for three or four weeks, and then carefully filtered before being used. In a well-stoppered bottle it will keep for years.

113. Mallory and Wright state that in Delafield's and Ehrlich's solutions it is well to mix the alum, hæmatoxylin, and water and leave them to oxidise for two or three weeks. The other ingredients appear to have a tendency to prevent oxidation and therefore to retard the ripening process.

Never put more than two or three sections at a time into the watch-glass, or they cling together, and are unequally stained. Use a weak stain, and stain slowly to get the best results. Should the staining be too intense, place the sections in a watch-glass, pour a few drops of strong acetic acid over them, then wash thoroughly and mount. v. Kahlden recommends that, for the purpose of getting rid of "over-stain," sections should be washed thoroughly in a 1 per cent. solution of acetic acid, and *then for from twelve to twenty-four hours in distilled water*. Specimens fixed in the chrome salts take on hæmatein slowly; those hardened in osmic acid still more slowly (one to six hours).

This thorough washing should be carried out in all cases where it is desired to obtain permanent preparations. For the use of eosin as a contrast stain, see § 132. Logwood or hæmatein stained specimens should be dehydrated in alcohol, cleared in clove oil (§ 193), and mounted in Canada balsam (§ 199).

114. *Anilin dyes.*—Thanks to the researches of Weigert, Ehrlich, Unna, and others, the anilin dyes are now largely used as staining reagents. These dyes are described as acid and basic salts of anilin

or toluidin or of both. The basic dyes act like carmine and logwood stains, picking out the chromatin of nuclei and staining bacteria. The acid dyes, picric acid, eosin, acid fuchsin, etc., appear to have an affinity for formed and dead tissues.

115. Of the basic dyes *methylene-blue* is probably used more than any other, not only as a nuclear and bacterial stain, but also as an excellent contrast stain. It may be used as a simple watery solution, 1-2 per cent. Another useful formula is—

Methylene-blue	1 part.
Alcohol, anhydrous	15 parts.
Distilled water	35 „

This is kept as a stock solution; when it is to be used, filter a few drops and dilute with about five times its volume of water. Muscle and other tissues may be mounted in glycerin (§ 194) or Farrant's solution (§ 195), or they may be counter-stained with eosin (§ 132), and mounted in Canada balsam (§ 199). Loeffler's methylene-blue solution is an excellent form in which to use this dye, as it remains unchanged for a considerable time.

Saturated alcoholic solution of methylene-blue .	30 parts.
Aqueous solution of caustic potash 1 : 10,000 .	10 „

Dehydrate and clear (§ 193), and mount in Canada balsam (§ 199). Toluidin-blue in watery solution may be used in place of methylene-blue, especially for nerve tissues, or when eosin or erythrosin is used as a contrast stain.

116. *Unna's alkaline methylene-blue solution*, first used to stain plasma cells, is now often used for general work with eosin as a contrast stain (§ 132).

Methylene-blue	1 part.
Carbonate of potassium	1 „
Water	100 parts.

Filter a few drops and, as required, add nine times the volume of water.

When this fluid is allowed to stand for some months, methyl-violet and a red stain are formed in the blue by a process of oxidation, and a

polychrome stain which often gives very beautiful results is obtained. Clear (§ 193) and mount in Canada balsam (§ 199).

117. *Methyl-violet* sometimes gives a double stain somewhat like the polychrome methylene-blue stain—red and blue. This appears to be the case only when the dye is impure, *i.e.* where there is a mixture of methylene-blue and methylene-red. Such a stain is most valuable as a stain for amyloid degeneration, the affected parts being most accurately differentiated from the normal tissues. The sections are placed in a watch-glass, with about half a drachm of the staining fluid of the watery solution of the ordinary methylanilin-violet of such a strength that when held up before the window in a three-quarter inch test-tube, light is allowed to pass readily. Leave the sections in this for two or three minutes; then wash well in water for half an hour, and mount in glycerin, either pure, or, as recommended by Cornil, slightly acidulated with acetic acid. Farrants's solution may also be used as a mounting medium. In any of the above media the stain is retained for a considerable time. Do not mount in dammar or Canada balsam, as both the clove oil and alcohol dissolve out the colour, and even the chloroform which is sometimes used as a solvent for the dammar or balsam dissolves out the methyl-violet freely, so that the colour, especially where the section has been imperfectly washed, is gradually discharged from the tissue, is diffused, and the section becomes blurred and muddy looking. Methyl-violet gives two reactions, a red-violet and a blue-violet; these are very well seen in hyaline cartilage, where the matrix takes on the red-violet stain, and the cells the blue-violet; or again, in "waxy degeneration," where the "waxy" material takes on the red-violet stain, whilst the healthy tissues take on a blue colour, in some instances almost a slaty blue. If it is not convenient to mount these stained sections at once, they may be kept in preservative fluid (§ 90), but not in alcohol, which discharges most of the colour from the tissues; even that which remains being diffused. For fresh tissues, epithelial structures, salivary corpuscles, or cells from the vagina or urethra, it is extremely useful. Used as a dilute watery solution (1 or 2 per cent.), it brings out nuclei and connective tissue corpuscles. Fresh tissues stained with methyl-violet should be mounted in "a saturated watery solution of potassic acetate." Methyl-violet is useful as a stain for micrococci and bacteria, which take it up and retain it firmly, even when washed in alcohol; and it may take the

place of gentian-violet in Ehrlich's anilin stains. Sections containing such organisms may be mounted in glycerin or Farrants's solution, after they have been well washed in very dilute acetic acid, or they *may* be washed in alcohol, clarified with clove oil and turpentine, and then mounted in dammar mounting fluid or Canada balsam (§ 199). Thierfelder recommends that specimens in which waxy degeneration is present should first be stained with the methyl-violet, and then washed in a saturated solution of oxalic acid, which discharges most of the colour from the normal tissues, leaving them a dull slaty grey, but intensifies or brightens the red violet stain of the waxy or amyloid tissues.

118. *Gentian-violet*, recommended by Weigert as a stain for tubercle bacilli, is prepared by adding 12 parts of a 2 per cent. watery solution of gentian-violet to 100 parts of a saturated solution of anilin oil water.

To prepare this saturated anilin oil water, take of

Anilin oil	1 part.
Distilled water	3 parts.

Shake well every half-hour for three or four hours, and decant the water as the anilin settles to the bottom. The commercial anilin is about a twelfth of the price of the purer anilin, but it is said not to answer the purpose so well. For ordinary staining with gentian-violet, a 2 per cent. watery solution, to which is added a crystal or two of thymol dissolved in alcohol, may be used. When mounting in xylol or benzol balsam, do not leave the section too long in either the alcohol or the oil of cloves, both of which reagents dissolve out the staining fluid very rapidly.

119. *Ehrlich* recommends a stronger solution; he uses 16 parts of a saturated alcoholic solution of gentian-violet to 84 parts of anilin water. The stain, prepared fresh every week twenty-four hours before use, should be carefully filtered. Probably the most stable of the gentian-violet preparations is Stirling's solution, which consists of—

Gentian-violet	5 parts.
Alcohol	10 „
Anilin	2 „
Water	88 „

In place of anilin water 5 *per cent.* watery carbolic acid may be used in the proportion of 90 parts of the carbolic acid water to 10 parts saturated alcoholic solution of the gentian-violet ; this, however, is not so reliable.

120. Basic fuchsin.—This solution is usually kept in stock as a saturated alcoholic solution.

The Ziehl-Neelsen carbol-fuchsin solution consists of—

Saturated alcoholic solution of fuchsin	10 parts.
5 per cent. carbolic acid water	90 „

Anilin fuchsin may be prepared in the same way as the anilin gentian-violet, 16 parts of the saturated alcoholic solution to 84 parts of anilin water. The fluid should always be filtered before use. It stains tissues very rapidly. It may be used as a stain for tubercle bacilli and for spores, which stain somewhat slowly and resist decolorisation by strong acids. Other bacteria take on this stain very rapidly.

121. Bismarck brown is an exceedingly useful contrast stain, especially for photographic work. It is invaluable for staining sections of bone and young granulation tissue. Take of—

Bismarck brown	1 part.
Alcohol, anhydrous	10 parts.
Distilled water	100 „

The sections must be stained slowly, and the water in which the staining fluid is suspended should contain about 10 per cent. of methylated spirit. Make a straw-coloured solution and allow the sections to remain in this for several days. Acid alcohol fixes the stain in the nuclei. Clear (§ 193) and mount in Canada balsam (§ 199) or glycerin (§ 194). Where used as a contrast stain, pour a few drops of the strong solution into a watch glass, and allow the section to remain in this for about ten minutes. This gives a very transparent brown colour to the nuclei and the margins of the cells, leaving the protoplasm almost unstained. When time is an element of importance, a stronger solution may be obtained by dissolving in boiling water or in 40 per cent. alcohol, either of which will take up 2 to 3 per cent. of Bismarck brown. Such a solution stains sections in about five minutes, after which they may be washed with absolute alcohol.

122. *Thionin-blue* may often be used in place of methylene-blue.

Thionin-blue	1	part.
Carbolic acid	2½	parts.
Water	100	„

When it is to be used, dilute with an equal volume of water and filter. Stain sections for from ten minutes to twenty-four hours. In order to bring out bacteria or nuclei, different degrees of decolorisation with weak acetic acid may be carried on, after which the section should be washed in water and then dehydrated with anilin oil, anilin oil and xylol equal parts, and finally xylol (§ 193); mount in xylol balsam (§ 199).

Muir (*Journ. Path. and Bact.*, Edinburgh, 1893, vol. v. p. 166) recommends that sections cut in paraffin may be stained by this solution or methylene-blue in the following manner: The sections, which should be thin, “after being cut and flattened in warm water, are placed on the surface of the staining solution for about half an hour. They are then washed well in water, placed on slides and allowed to dry. The paraffin is then removed by xylol and the section is mounted. . . . One or two trials with any stain are necessary to determine the length of time which gives the best results.” This same solution may be used in staining blood preparations.

Hoyer recommends the use of thionin for the staining of mucus. Place the specimen in a dilute aqueous solution of thionin (2 drops of a saturated aqueous solution to 5 c.c. of water) for from five to fifteen minutes. Dehydrate rapidly in absolute alcohol, clear with xylol (§ 193), and mount in balsam (§ 199). The characteristic intense red colour is best brought out, however, by mounting the sections in glycerin (§ 194). Tissues should be hardened or soaked in sublimate before being placed to stain in this solution.

123. *Victoria-blue* is slightly soluble in water and very soluble in alcohol. Either of these solutions may be used for the staining of elastic bundles in preparations fixed in Flemming's solution (§ 70). Wash the sections in alcohol or decolorise with Gram's fluid. This stain has also been used by Bolles-Lee as a nuclear stain. The sections of tissues hardened in Hermann's fluid (§ 70a) are soaked in Lugol's solution (§ 42) for fifteen minutes; they are then stained, first for eighteen hours in a concentrated watery solution of Victoria-blue

and then for ten minutes in a watery solution of methyl-orange, followed by immersion for ten minutes in a $\frac{1}{2}$ per cent. solution of acid fuchsin ; wash in alcohol and clear (§ 193), and mount (§ 199).

124. *Safranin* is a very good stain. Safranin O, soluble in water, and especially in hot water, is used for nerve tissues. Safranin, soluble in alcohol, is specially useful for bringing out nuclear figures in fresh tissues or in tissues that have been hardened in Flemming's solution (§ 70), bichloride of mercury (§ 61), etc. Dissolve

Safranin	1 part.
In alcohol	100 parts.

Allow to stand for several days, then add 200 parts of water. Stain the sections in the solution for twenty-four hours, wash thoroughly in water, and remove any excess of stain from the tissues with absolute alcohol, examining the sections on the slide under the microscope from time to time as the process of decolorisation is proceeding. Clear (§ 193) and mount in Canada balsam (§ 199).

Instead of the above mixture Mallory and Wright recommend a mixture of equal parts of

- A saturated aqueous solution of safranin O, soluble in water ;
- A saturated alcoholic solution of safranin soluble in alcohol,

used as a nuclear stain to bring out karyomitotic figures ; it is applied for from five minutes to twenty-four hours, according to the strength of the solution used. The sections are next rinsed in water, then in 95 per cent. alcohol, to which are added a few drops of acid alcohol, then in turn in 95 per cent. alcohol, and finally in absolute alcohol ; clear in xylol (§ 193) and mount in xylol balsam (§ 199).

Mallory and Wright recommend that the section should be stained very deeply, then treated with alcohol slightly acidulated with hydrochloric acid, which although it takes the stain out of the resting nuclei leaves the chromatosomes deeply stained.

125. *Babes' anilin safranin* is said to stain very well and rapidly, and will remain stable for a couple of months.

Two per cent. anilin water is saturated with safranin O by heating in a flask in a water-bath raised to 80° C. ; filter. If the specimen is stained in bulk, the excess of stain should be removed by soaking the

piece of stained tissue in a 0·5 per cent. solution of hydrochloric acid in absolute alcohol. By this method the active nuclei are stained bright red, the resting nuclei much less brightly. Safranin stains fibrous tissue.

Safranin is useful for material that has been hardened with osmic acid, especially when the osmic acid is left in the tissues.

126. *Benda's stain*—

- (1) Saturated solution of safranin O in saturated anilin water.
- (2) "Light green" 3·5 to 0·25 per cent. in 80 per cent. alcohol.

Filter a few drops of solution (1) on to the preparation, allow to stain for from fifteen minutes to three hours, wash with water, then decolorise with "light green" solution as follows:—

Filter the "light green" on to the preparation, and gently run the fluid backward and forward over it; run off and repeat this until the tissues take a light green tint, rinse with methylated spirit and examine under the low power. If there is too much safranin wash further with methylated spirit, dehydrate, preferably by blotting; when the exact tint has been obtained, clear with xylol (§ 193), and mount in xylol balsam (§ 199). This method of staining has been very successful in connection with the demonstration of the amœbæ found in dysenteric amœbic abscesses. It is also useful in the staining of inflammatory cells, especially those found in the peritoneal cavity, in experimental work.

127. Or similar tissues after being fixed in *Mann's fluid*—

Formalin	20 parts,
Sodium chloride	1 part,
Distilled water	70 parts,

for twenty-four hours, are transferred to 75 per cent. alcohol. Sections are stained in fuchsin or safranin (§ 120 or 124) and differentiated with 95 per cent. alcohol, to which have been added a few drops of acid alcohol (prepared by adding 1 per cent. hydrochloric acid to 70 per cent. alcohol), till they are pale pink to the naked eye; wash well in 90 per cent. alcohol, and stain for half a minute in

Light green	0·5 part.
Alcohol	200 parts.

128. *Anilin blue-black* is especially useful for staining sections of the nerve centres, bringing into special prominence the nerve cells, which are stained a slaty blue colour (Bevan Lewis).

It is made as follows:—Take of

Anilin blue-black	1 part.
Water	40 parts.
Dissolve and add rectified spirit	100 „

Keep in a stoppered bottle, filter a few drops into a watch-glass, and add eight or ten volumes of alcohol. Stain the section for from a half to three minutes, and mount in Canada balsam (§ 199). For ordinary tissues use a 1 per cent. watery solution, allow the sections to remain in this for a few minutes, and mount in balsam. If the staining is too deep, Stirling recommends soaking of the sections for a time in a 2 per cent. solution of chloral hydrate.

129. Bevan Lewis's special method of staining fresh nerve tissues: Freeze a piece of fresh brain or cord in gum on an ether microtome. Cut sections and remove them one by one into cold water, from which spread out at once on a glass slide. With a pipette pour on each a few drops of a 2 per cent. osmic acid solution; leave the sections in this for from one to two minutes, then wash thoroughly in water, and stain on the slide with the 1 per cent. solution of anilin blue-black (§ 128) for one or two hours. Examine at once or mount in acetate of potash or glycerin (§ 194). Sections which are to be mounted in balsam should first be well washed in water, then allowed to dry thoroughly (well protected from the dust), covered with balsam and mounted.

130. *Methyl-green*.—As a 1 per cent. watery solution this gives a beautiful rose pink reaction with waxy material, staining the normal tissue a bluish-green. Bolles-Lee points out that this reagent has several additional advantages. It does not over-stain; it is very penetrating, kills cells instantly without causing swelling or other change of form, and preserves them for several hours. It may also, with advantage, be combined with weak solutions (0.1 to 1 per cent.), of osmic acid, by which mixture tissues are both fixed and double stained. Mount in xylol balsam (§ 199), but remember that alcohol dissolves out this stain very rapidly, hence the section should not

remain very long in this fluid, nor should it remain long in the clove oil, which also quickly discharges the colour. It forms an excellent contrast stain for the tissues around the tubercle bacillus stained with basic fuchsin.

131. Diffuse stains.—*Picric acid* has already been referred to (§§ 102, 103, and 104).

Fuchsin.—A concentrated watery solution of acid fuchsin should be prepared by those who intend to investigate the pathology of the nerve centres. It is also used in the preparation of van Gieson's fluid (§ 103).

132. Eosin used as a $\frac{1}{10}$ per cent. solution gives a beautiful transparent stain, which will remain unaltered for a considerable length of time. It may be used in watery solution, especially for muscular tissue of the heart, etc., or as an alcoholic solution for staining other tissues and blood corpuscles. To stain with eosin, filter a few drops of the solution into a watch-glass containing distilled water, place the sections in this, and allow them to remain for a minute or two, wash in water slightly acidulated with acetic acid, mount in balsam (§ 199), Farrant's medium (§ 195) or acidulated glycerin (§ 194). It forms an excellent contrast stain to methylene-blue in Jenner's (§ 151), Leishman's (§ 153), and the other double stains. Sections stained with hæmatoxylin or hæmatein (§ 108 *et seq.*), after being thoroughly washed in water, are stained in eosin-alcohol until they take on a pale red colour; clear in xylol (§ 193), and mount in Canada balsam (§ 199).

Guipel recommends that sections of tissues hardened in corrosive sublimate, after being stained in hæmatein or hæmatoxylin, should be over-stained in a saturated alcoholic solution of eosin to which an equal volume of water has been added. They are then washed in water until no more colour comes away, cleared and mounted as above. Here as with thionin, it is well to place the sections in corrosive sublimate solution before the stain is applied. Tissues in which there is no excess of chrome salts, after being stained with methylene-blue and thoroughly washed in water, may be stained in eosin-alcohol until they take on a pale red tinge. Clear in xylol (§ 193) and mount in balsam (§ 199).

Eosin may be used as a counter stain for sections which have been stained with methylene-blue. Stain somewhat deeply in methylene-blue, then wash in eosin-alcohol until the sections take on a pale red tinge. Clear in xylol (§ 193) and mount in balsam (§ 199). Specimens

kept for a long time in chrome salt solution are not readily stained by this method.

SPECIAL STAINS

133. *Iodine staining solution* in the form of Lugol's solution (§ 42) (of a dark sherry or brown vinegar colour) should never be very strong for microscopic work. Waxy tissues stained with this reagent appear rich mahogany brown when the section is examined by reflected light, the normal tissues yellow; when examined by transmitted light, however, the waxy material assumes a lighter yellow than the surrounding healthy tissues, than which it is much more translucent. It must be remembered that the granules of glycogen in liver cells assume the same mahogany brown colour when stained with iodine solution, as do also some of the cells in growing bone and the granules in certain leucocytes. To stain a section, place it in a watch-glass, and pour over it a small quantity of the solution; allow it to stand for ten minutes; wash rapidly in water, and mount in iodine mounting fluid (see below)—never in Farrants's solution or glycerin, or the staining fades, the iodine diffusing rapidly into the mounting medium. Another method is to float out the section on a slide, and drop a small quantity of the fluid on to it with the glass rod; allow this to stand for a few minutes, then a drop of the mounting fluid is added, and the cover-glass is lowered on to the specimen. Where iodine is used the solution in which the section is mounted must be kept saturated with iodine, and as this is very volatile, the cover-glass must be cemented at once with French glue, Canada balsam, or some such cementing substance.

To make the iodine mounting fluid, take of

Liquor iodi (B.P.)	3½ parts.
Glycerin	6 „
Water	6 „
Mix, and add, carefully picked gum arabic,						
about	6 „

Keep in a stoppered bottle, stirring or shaking regularly, until the whole of the gum is dissolved. Allow the fluid to stand until all air-bubbles have risen to the surface, and then decant into a small stoppered bottle to the stopper of which a glass rod is fused (§ 206).

133*a*. The iodine reaction with certain granules found in leucocytes is best obtained by the use of Ehrlich's original method. He takes of—

Iodine	1 part.
Potassium iodide	3 parts.
Distilled water	100 „
Gum acacia, sufficient to convert the fluid to the consistence of a thin syrup.	

A blood film dried in the air is mounted in, and simultaneously stained by, this solution; use as small a quantity as possible in mounting, in order to avoid rendering the specimen opaque. The preparation, though by no means permanent, does not deteriorate appreciably for several weeks (Barnicot).

134. To obtain the blue reaction with *iodine and sulphuric acid* in waxy organs, treat fresh sections in a conical test glass with a dilute watery solution of iodine for about half an hour; then immerse them in a 4 per cent. solution of sulphuric acid until a blue colour makes its appearance. Mount in glycerin (§ 194) or Farrants's solution (§ 195). This is an extremely delicate test for waxy material, but unfortunately it is not always successful, though in the hands of some observers, especially with fresh material, extremely satisfactory results have been obtained.

135. *Osmic acid*, perhaps the most delicate of all staining reagents, is invaluable for staining fat and nerve fibres. It may be kept as a 1 per cent. watery solution, made by breaking the glass tube in which it is supplied in a mortar, and triturating with 100 parts of distilled water. It should be kept cool in a glass-stoppered bottle, well protected from the light by a covering of brown paper closely gummed to the bottle. It may afterwards be diluted as required.

When required as a staining reagent it is used as a $\frac{1}{2}$ to $\frac{1}{6}$ per cent. solution. The sections to be stained are placed in a small quantity of the fluid carefully protected from the light, and left for from one to twelve hours, after which they are washed in distilled water, and mounted in Farrants's solution (§ 195) or glycerin (§ 194); never in Canada balsam or dammar, unless these are dissolved in chloroform only. Clear with chloroform, as xylol dissolves osmic acid. Sections thus stained may afterwards be stained with alum carmine (§ 106). Osmic acid blackens fat, the myelin of white nerve fibres,

the outlines of fibres, and cells, at the same time giving the substance of these structures a greenish-grey or olive-green tinge. In the various hardening fluids into the composition of which it enters (§§ 69 to 70*b*) it also acts as a staining reagent.

135*a*. *Sudan III.*, which is insoluble in water but soluble in alcohol and fats, may be used to stain fatty tissues hardened in the formalin or formalin-Müller group of hardening reagents and cut on the freezing microtome. Wash the sections thoroughly in water, and then transfer to 50 per cent. alcohol. Make a saturated solution of the Sudan III. in hot 70 per cent. alcohol; filter into a watch-glass, and allow the sections to remain in this stain for half an hour; rinse in 50 per cent. alcohol, and wash thoroughly in distilled water; counterstain with hæmatoxylin (§ 109 or 110), and mount in glycerin (§ 194), or Farrants's solution (§ 195).

135*b*. In place of Sudan III., Scharlach R may be used. Herxheimer recommends the following solution:—

Absolute alcohol	70 parts.
Aq. dest.	10 „
10 per cent. watery solution of sodium hydrate						20 „

Add Scharlach R to saturation. Stain for two or three minutes, and then treat the section as when Sudan III. is used.

136. *Gold chloride* is of comparatively little use to the pathologist, except in the case of tissues which can be transferred whilst living to the staining fluid. In the examination of the morbid conditions of the cornea it is, however, an extremely valuable reagent, as also in the examination of tumours and of the axis cylinders of nerves and nerve terminations in muscles which have been removed from the body during life, and in tissue degeneration. It should be remembered that it can be used to best effect only within a quarter of an hour of the removal of the part from the living body, and that it acts as a fixing and hardening solution as well as a stain. It may be used in any of the following ways:—

(*a*) Soak the tissue as soon as removed from the body in a $\frac{1}{2}$ per cent. solution of chloride of gold, until it assumes a lemon colour; then expose in 1 per cent. acetic acid solution to strong light, until it

assumes a purplish tinge. Sections thus prepared show connective tissue corpuscles (corneal corpuscles, cartilage cells), nerve fibrils, especially those of small size, and ganglion cells, stained reddish-purple. Mount in glycerin (§ 194).

(b) Ranvier's original lemon juice and gold method gave extremely good results; but it has been superseded by his formic acid method.

Chloride of gold, 1 per cent. solution . . . 8 parts.

Formic acid 2 „

Boil, allow to cool, and immerse the tissue in it for one hour, in the dark. *Small thin* pieces should be used; wash quickly in water, and transfer to a mixture of formic acid 1 part; water 4 parts, exposing the vessel to diffused light for twenty-four to forty-eight hours. Harden in the dark in gradually increasing strengths of alcohol (§ 60).

Löwit also recommends a formic acid method. In diffused light place a *very small* piece of *fresh tissue* in formic acid 1 part; distilled water 1-2 parts, until it becomes transparent. Transfer to chloride of gold 1 to 1.5 part in 100 parts of water for fifteen minutes; then to 25 per cent. solution of formic acid for twenty-four hours, and again to concentrated formic acid for twenty-four hours. Preserve in glycerin. All the processes except the first should be carried out in the dark, and the tissue should be protected from the light throughout.

(c) An exceedingly good form of the gold method, especially for nerve tissues, is Beckwith's modification of Freud's method.

Pieces of nerve centres, or nerves, are hardened (*not* over-hardened) in Erlicki's fluid (§ 66), and then, though not necessarily, in alcohol. Sections rinsed with water are placed for three or four hours in a 1 per cent. solution of gold chloride, after which they are washed with water, treated with a 20 per cent. solution of caustic soda for three minutes, then with a 10 per cent. solution of carbonate of potash for thirty minutes; the superfluous fluid is then drained off, and the sections are placed for from five to fifteen minutes in a 10 per cent. solution of iodide of potassium. They are washed in water, dehydrated, and mounted in balsam.

This method gives most beautiful results, picking out the delicate nerve fibrils and axis cylinders in a most remarkable manner. One of the main factors of success is that the specimens should be taken

directly into the gold solution, the knife being wetted with water instead of with alcohol.

137. *Nitrate of silver* is used specially to bring out the intercellular substance on any epithelial or endothelial surface, *e.g.* peritoneum, blood vessels, lymphatics, etc., which may be injected with a weak silver nitrate solution; this is reduced by light to the black oxide of silver. It is also used as a stain for the intercellular substance of cartilage, and for the laminated intercellular tissue of the cornea, though, if the tissues be exposed for a considerable time in the silver solution, the nuclei, and even the protoplasm of connective tissue, epithelial or fat cells may become more or less blackened. To the pathologist it is specially useful in the study of the eye and of tumours of epithelial type, as most other tissues have been dead for some time before they come into his hands. For demonstrating the structure and relations of the alveoli of cancerous growths, this reagent is perhaps the most valuable at command. Take a very thin section of the tissue to be stained as soon as it is removed from the body, keep it fully stretched, and wash well in distilled water to remove all chlorides, which would at once throw down the silver as a white precipitate. Expose it to the action of a large quantity of $\frac{1}{2}$ or $\frac{1}{4}$ per cent. solution of nitrate of silver for one or two minutes (until it becomes somewhat whitened); wash in water (not distilled), and expose to diffuse daylight until a delicate brown colour makes its appearance. Care must be taken to protect the specimen from the direct action of the sun's rays, or the tissues soon become quite opaque and very deeply stained. Preserve these specimens (if not mounted at once) in a mixture of glycerin 2 parts, and water 1 part, to each ounce of which have been added 5 to 10 drops of acetic acid. These stained sections may also be preserved in a mixture of equal parts of spirit and glycerin. Mount in glycerin (§ 194).

138. Hamilton recommends the following method for the study of inflammation in the cornea. Chloroform the animal—kitten or summer frog. With a pointed stick of lunar caustic, or a glass tube containing and protecting a small pledget of cotton wadding soaked in 10 per cent. nitrate of silver solution, touch the cornea, removing the surface epithelium over a small area. Neutralise the nitrate of silver by washing the surface of the eye with 5 per cent. common salt solution. Before killing the

animal at the time required (three hours to several days) again chloroform it and rub over the whole corneal surface with lunar caustic, or the anterior surface may be scraped to remove the epithelium, and then bathed with a 10 per cent. aqueous solution of nitrate of silver until the cornea becomes milky. In the latter case it should, after being excised, be laid in the silver solution for a few minutes. Then wash thoroughly in normal salt solution and expose to diffuse daylight for half an hour. Transfer to the acidulated glycerin solution for twenty-four hours. Cut sections on the freezing microtome, first making two to four incisions at the margin, so that the cornea may lie flat on the freezing disc. Stain in Delafield's hæmatoxylin solution (§ 109 (c)). Mallory and Wright, in order to avoid the shrinkage caused by the use of strong alcohol, recommend that the sections should be dehydrated in 50 per cent. and then in 70 per cent. alcohol, after which they should be cleared in anilin oil and xylol (§ 193) and mounted in balsam (§ 199). For rapid work Hamilton's method of placing the excised cornea in 1 per cent. acetic acid until it swells up to several times its normal thickness may be used, especially when the tissue is to be simply delaminated.

139. Iron salts.—Dr. Elizabeth Hoggan recommends that sections of epithelioma, papilloma, etc., after being treated with water and a dilute solution of nitrate of silver and methylated spirit, should be left for a time in a 2 per cent. solution of perchloride of iron, and lastly, in a 2 per cent. solution of pyrogallic acid. The nuclei of epithelial cells are stained very distinctly, and the processes of the prickle cells of papillomas are well brought out. A weak solution of tannic acid or of gallic acid in alcohol may be used instead of the pyrogallic acid for the purpose of reducing the iron salt. The weaker the solution and the longer the time required for the reduction, the better are the results obtained.

Nuclear black is really an ink of which the composition has not been made known, though it is said to consist of iron combined with some organic acid. It can only be obtained in solution. When diluted it acts specially as a very fine nuclear stain, also picking out the axis cylinders of nerves. Undiluted it acts upon the protoplasm of cells, connective tissues, and medullary sheaths of nerves. Differentiation is effected by alkalis or acid alcohol. Bolles-Lee recommends its use for the study of the protoplasm of cells. Fix in Flemming's solution and stain

sections for a couple of hours in the nuclear black, wash for two or three minutes in dilute lithium carbonate, counterstain in a concentrated watery solution of Victoria-blue, then differentiate in alcohol, clear (§ 193) and mount (§ 199). Iron is also used for mordanting and differentiating hæmatoxylin stained specimens in which it is desired to bring out the nucleus. Heidenhain, after mordanting the tissue in a 3 per cent. aqueous solution of ferric ammonium sulphate, washes thoroughly in distilled water and then transfers to a $\frac{1}{2}$ per cent. aqueous hæmatoxylin solution, where it may be left for from a half to two or even eighteen hours. The sections are again thoroughly washed in ordinary tap water and transferred to the ferric ammonium sulphate solution until the section becomes grey. Under the microscope the nuclear chromatin should be deep blue, the protoplasm colourless. Wash thoroughly in water, dehydrate in alcohol, clear in xylol, and mount in balsam. Mallory uses as his mordanting and differentiating fluid a 10 per cent. aqueous tincture of perchloride of iron which is allowed to act for from three to five minutes. Blot the section and stain for from three to five minutes in a 1 per cent. watery solution of hæmatoxylin crystals, taking care to have an excess of the staining fluid. Wash well in water, stain deeply, and decolorise slowly; then differentiate in a 0.25 per cent. aqueous solution of ferric chloride (a few seconds to two minutes), care being taken to keep the sections "constantly moving" in the solution; wash in water. Dehydrate in alcohol and clear in origanum oil (§ 193), and mount in balsam (§ 199); see also § 110 (a).

140. *Weigert's method for central nerve tissues.*—Stain a section hardened in Müller's fluid (§ 62) or Erlicki's fluid (§ 66) for twenty-four hours in a concentrated watery solution of acid fuchsin (soda salt of rose anilin sulphate). Wash in water and transfer to an alkaline solution of alcohol "(namely, 100 c.c. of absolute alcohol with 10 c.c. of a solution made by dissolving 1 grm. of fused caustic potash in 100 c.c. of absolute alcohol, and filtering) for a few seconds, until the first sign of the grey nerve tissue of the section becomes visible"; wash in water, "which must not be acid," and dehydrate with absolute alcohol saturated with sodium chloride, to preserve the colour of the section. Clear with oil of cloves, and mount in Canada balsam (§ 199). In sections prepared in this manner, the medullated nerve fibres, even those in the anterior horns of the spinal cord, stand out as brilliant red lines or points. The sheath, or part of the sheath, is stained by this

method. "The ganglion cells and connective tissue (especially in sclerosis), with the pia mater, vary in tint from a pale to an exquisite blue, which latter is increased by rinsing the sections in a solution of 1 part of hydrochloric acid to 5 of water, and then washing thoroughly in water before dehydrating them with alcohol. These tissues can also be stained blue by hæmatoxylin," "before or after colouring with the acid fuchsin."

Weiger's method of mordanting and staining the myelin sheath of the nerves of the nerve centres; the sheath taking on a blue stain, the neuroglia light yellow, and the ganglion cells a brown tint. After the tissues have been thoroughly fixed in a 4 per cent. solution of formalin (four days for pieces not over $\frac{1}{3}$ inch thick) changed every twenty-four hours, they are mordanted in the following solution for four days, and no longer:—

Bichromate of potassium	5 parts.
Chrome alum	2 „
Water	100 „

Keep in 80 per cent. alcohol, and in the dark, changing the alcohol as it becomes coloured. A piece of this tissue, embedded in celloidin (§ 91) is then transferred to the following mixture:—

Acetate of copper	5 parts.
Acetic acid, 36 per cent. solution	5 „
Chrome alum	2.5 „
Water to	100 „

Boil the chrome alum and water in a covered dish until it turns green. Stop the boiling, add the acetic acid, and then the acetate of copper. Stir briskly until everything is dissolved, and then cool. There should be no green precipitate. The tissues become green, and the celloidin bluish-green. Take of

A. Water	90 parts.
Saturated solution of lithium carbonate	1 part.
B. Hæmatoxylin	1 „
Absolute alcohol	10 parts.

When required, mix equal parts of A and B, and dilute somewhat. Leave the sections in this solution for any length of time between one

and twenty-four hours, taking care to keep the temperature between 35° and 45° C. Wash well in water, and transfer to a solution of

Borax	2 parts.
Ferrocyanide of potassium	$2\frac{1}{2}$ „
Water	100 „

Allow the sections to remain in this for from half an hour to two or three hours until the grey substance is distinctly yellow, the time varying according to the thickness of the section and the intensity of the logwood stain. Again wash well in water, dehydrate in strong spirit, clear in a mixture of anilin oil 2 parts and xylol 1 part (§ 193), and mount in Canada balsam (§ 199) or dammar mounting fluid.

141. Pal's modification of Weigert's method.—Pal uses the same hæmatoxylin staining fluid, but afterwards transfers his sections (previously washed in water to which has been added 1 to 3 per cent. of a saturated lithium carbonate solution, until the section assumes a uniform deep blue colour) for from twenty seconds to five minutes into a freshly prepared $\frac{1}{4}$ per cent. solution of permanganate of potash, until the grey matter looks brownish-yellow, and then to the following:—

Oxalic acid (pure)	1 part,
Sulphite of potash	1 „
Distilled water	200 parts,

for a few seconds, until the “grey” matter loses all colour, the “white” matter remaining moderately deeply stained blue. Wash thoroughly in water, dehydrate in strong spirit, clear in anilin oil and xylol (§ 193), and mount in Canada balsam (§ 199), or give a contrast stain with eosin (§ 132) or picro-carmin (§ 102). Pal gives a special formula for the hæmatoxylin solution, but it appears to have no special advantage over Weigert's solution. This stain is specially useful for thick sections and for large nerves, but is not so good as Weigert's method, when the finer nerve sheaths have to be differentiated.

142. The Pal-Exner method.—This method is specially valuable for obtaining stained sections rapidly. Fresh brain or cord is hardened for two days in ten times its bulk of $\frac{1}{2}$ per cent. osmic acid solution; fresh solution is added on the second day. The specimen is then washed carefully in water, placed for a short time in absolute alcohol, and embedded in celloidin or paraffin. The sections are put into

glycerin, washed in water, stained and differentiated by Pal's method, and mounted in the usual manner.

143. *Modification of Golgi's method of demonstrating nerve cells with axis cylinders and dendritic processes (Kallius).*—This method is more suitable for pathological work than is Golgi's original method, and it possesses the great advantage that the preparation so made may be protected by a cover-glass.

(a) Harden in Müller's fluid (§ 62), (in brown glass vessels, for from one to three months according to temperature, increasing the amount of bichromate every eight days from 3·5 up to 5 grms. per 100 c.c. of distilled water) or in Erlicki's fluid (§ 66), wash rapidly in distilled water, and place in $\frac{1}{2}$ to 1 per cent. solution of nitrate of silver for from twenty-four to forty-eight hours, changing the solution when it becomes yellowish.

Sections of the tissue (which should be thinner than the sections to be prepared by any of the ordinary Golgi methods) should be washed well in alcohol to remove any excess of silver nitrate.

Prepare an ordinary hydrokinone photographic developer, namely,

Hydrokinone	1 part,
Sulphite of soda	8 parts,
Carbonate of potash	1·5 part,
Distilled water	50 parts.

(b) Dilute one part of the developer with 12·5 parts of water, and allow to stand for two or three days in the dark (it will keep for several weeks). Into a portion of this diluted developer, to which has been added one-third its volume or even an equal volume of absolute alcohol, place the sections and leave them until they have assumed a very dark grey tint. If any precipitate is thrown down, due to excess of alcohol, add a few drops of the developer. Transfer to 70 per cent. alcohol, where they are allowed to remain for ten or fifteen minutes, after which they are "fixed" in a 20 per cent. aqueous solution of hyposulphite of soda. Then wash as you would a photographic negative in running water for twenty-four hours. Dehydrate and clear (§ 193) and mount in Canada balsam (§ 199).

144. *Nissl's stain for protoplasmic granules in nerve cells.*—Harden small pieces of tissue $\frac{1}{3}$ to $\frac{1}{2}$ inch in diameter in 90 per

cent. alcohol for two or three days, four at the outside. Remove the excess of alcohol with clean blotting paper, fix to a block with thick celloidin, which should be used as a cement only, and put to harden in strong spirit—90 per cent. Whilst cutting, keep the knife moistened with this spirit. Sections, which should be about $10\ \mu$ thick, should be preserved in strong spirit. Stain in solution A, which should be raised to a temperature of 60° – 70° C.

Solution A.

Methylene-blue, B., patent	3.75 parts.
Venetian soap	1.75 part.
Distilled water	1000 parts.

(In this solution thionin may be used instead of methylene-blue.) Partially decolorise, *i.e.* until only a faint trace of colour comes away in

Solution B.

Anilin oil	10 parts.
Strong alcohol (96 per cent.)	90 „

“Blot” section on the slide with clean filter paper and cover with oil of cajeput. Again blot with filter paper; then run a few drops of benzine over the section. Add a few drops of benzine-colophonium (made by dissolving colophonium in benzine for twenty-four hours and then decanting). Pass the slide through a flame to drive off the benzine, blowing out the flaming benzine at once. Repeat this until the whole of the benzine is driven off; put on a cover glass, and warm the slide until the cover slip falls into position and the colophonium is spread out in an even layer. Water, ether, etc., should never be allowed to come in contact with this tissue. As the colour does not diffuse into the solid colophonium, these preparations retain their stain indefinitely.

A simpler method of staining Nissl's granules is that devised by Juliusburger and Meyer: Harden small pieces of the tissue in Müller-formalin solution in the cold. Freeze or embed in celloidin. Stain sections in a 1 per cent. warm aqueous solution of thionin-blue (§ 122) for from a half to one minute. Decolorise in strong alcohol, examining the specimen from time to time in bergamot oil (§ 193) under the microscope until the proper differentiation of the Nissl's

bodies—which should be blue—is obtained, and mount in carbol-xylol balsam (§ 199).

145. Stains for the neuroglia of the central nervous system may be used in cases where the tissues can be obtained within two or three hours of the death of the patient. After this some change takes place in the chemical composition of the neuroglia, as a result of which they no longer take on the characteristic stain at the end of twenty-four hours. A capital method, devised by Mallory, is the following. After fixing small pieces of the tissue in a 4 per cent. aqueous solution of formaldehyde for four days, transfer to a saturated aqueous solution of picric acid; leave in this for four days, and then harden in a 5 per cent. aqueous solution of bichloride of ammonia for from four to six days in an incubator, or for as many weeks at the ordinary room temperature. Transfer to alcohol; embed in celloidin. Cut sections and place them in a $\frac{1}{2}$ per cent. aqueous solution of permanganate of potash for from fifteen to thirty minutes; wash in water, then rinse for fifteen or thirty minutes in a 1 per cent. aqueous solution of oxalic acid. Wash thoroughly in water and stain in phosphotungstic-acid hæmatoxylin (Mallory) for one or two days.

This stain is prepared as follows:—

Hæmatoxylin	0·1 part.
Water	80 parts.
10 per cent. aqueous solution of phosphotung-	
stic acid (Merck)	20 „
Peroxide of hydrogen (B.P.)	0·2 part.

Dissolve the hæmatoxylin in a little heated water, cool and add to the rest of the solution. The mixture may be used at once, but it keeps well without the addition of any antiseptic. *Rinse* the sections quickly in water, dehydrate as quickly as possible in 95 per cent. alcohol, clear in origanum oil (§ 193), and mount in xylol balsam (§ 199).

“Nuclei, neuroglia fibres and fibrin stain blue; axis cylinders and ganglion cells, pale pink; connective tissue, deep pink. The blue colour is a little sensitive to strong light and on prolonged exposure will fade to pink.

“If a permanent isolated stain of the neuroglia fibres is desired, place the sections (after staining as above directed in the phosphotungstic-acid hæmatoxylin and washing in water) in a 30 per cent. alcoholic

solution of ferric chloride for from five to twenty minutes (rarely longer), then wash in water and dehydrate as before. The nuclei, neuroglia fibres and fibrin stand out sharply, of a clear blue colour; everything else is decolorised or appears of a pale yellowish or greyish tint."

146. *To demonstrate the Negri bodies in the brain of a rabid animal.*

—Williams and Lowden recommend the following method for diagnostic purposes. A fragment of the grey substance from the cerebral cortex in the region of the fissure of Rolando, another from the cornu ammonis, and a third from the cerebellum, is taken from a section made at right angles to the surface, and placed on a slide about 1 inch from the end. A coverslip is now "pressed upon it until it is spread out in a moderately thin layer; then the coverslip is moved slowly and evenly over the slide," leaving the first $\frac{3}{4}$ or 1 inch of the slide clean. Use slight pressure in making the smear, pressing rather more on the edge of the coverslip away from the end of the slide towards which the coverslip is travelling, thus driving more of the nerve tissue along the smear, "and producing more well-spread nerve cells," dry in air and then stain by one of the following methods (a) or (b).

(a) Fix in methyl alcohol for about five minutes, and stain in Giemsa's solution (§ 157). Ten drops of the stain added to 10 c.c. of distilled water made alkaline by the previous addition of 1 drop of a 1 per cent. solution of potassium carbonate, is poured over the slide and allowed to stand for from a half to three hours. The organisms are not over-stained even after twenty-four hours. Wash in tap-water for two or three minutes, drain, and dry with filter paper. If the smear is thick, the specimen may be dipped into 50 per cent. methyl alcohol before it is washed in water. A stronger solution of the Giemsa's stain of course acts more rapidly. The cytoplasm of the Negri body stains blue, the central body and chromatoid granules a blue-red. The larger bodies have usually a somewhat darker blue than the smaller; the nuclei of the nerve cells are stained red, the nucleoli a dull blue.

(b) Van Gieson uses the following in place of Giemsa's stain: To 10 c.c. of distilled water 3 drops of a saturated alcoholic solution of rose aniline violet and 6 drops of Loeffler's solution of methylene-blue (§ 115) are added. This stain, poured on to smears that have been fixed in methyl alcohol for one minute, is warmed until steam rises. It is then poured off and the specimen is rinsed in water and allowed to dry. The staining solution should be prepared fresh each

time it is used, as it does not remain good for more than about an hour.

(c) Mallory's method given below may also be used for smears fixed in Zenker's fluid (§ 63) for half an hour, and then passed through iodised alcohol and alcohol.

When it is desired to examine the bodies *in situ* in sections, small pieces of the grey matter taken from the above positions are immersed in Zenker's fluid (§ 63) for *three or four hours*. They are then washed in running water for five minutes, after which they are placed in 80 per cent. alcohol, to which enough tincture of iodine has been added to give a port-wine colour, for about twenty-four hours; then in a similar iodine 95 per cent. alcohol for twenty-four hours; then 95 per cent. alcohol for twenty-four hours, absolute alcohol from four to six hours, after which they are left in cedar oil until they are clear, then in equal parts of cedar oil and paraffin melted at 52° C. for two hours. They are then embedded in paraffin (§ 94). Sections are cut, fixed to the slide (§ 98), and, after the paraffin has been removed from them, washed in absolute alcohol. They are then stained with eosin (§ 132) for twenty minutes, rinsed in tap-water, counterstained with methylene-blue solution (§ 115) fifteen minutes, differentiated in 95 per cent. alcohol for from one to five minutes, and dried with filter paper. The cytoplasm of the body is a magenta colour, light in the small bodies, dark in the larger; the central bodies and chromatoid granules are very dark blue, the nerve-cell cytoplasm a light blue, the nucleus a darker blue, and the red blood cells a brilliant eosin tint.

147. *Special triple stain for bones and other sections which are to be photographed.*—Ehrlich's triple stain is specially valuable for photographic work—

A. Ehrlich's acid hæmatoxylin.

B. Make a saturated watery solution of Rubin S. (One of the fuchsin series.)

C. Make a similar solution of methyl-orange. (A good "ground" stain.)

Stain the sections in a mixture of equal volumes of the logwood (filtered when used) and distilled water for from five to fifteen minutes, wash well in distilled water and, if necessary, with very dilute acetic acid, to discharge the stain from everything but the nuclei; then leave in tap-

water until the desired shade of blue is obtained, or wash with a *very dilute* solution of ammonia, avoiding precipitation as far as possible. Then place in a watch-glass containing equal proportions of *B* and *C* for from ten to thirty minutes; wash freely in ordinary water, dehydrate and mount in Canada balsam.

This method is exceedingly useful for decalcified bones, and for other tissues where it is desirable to obtain good contrasts.

148. Ehrlich's modification of the Biondi-Heidenhain triple stain.

—This stain is specially useful in the study of blood, though it may be used to stain epithelial and other cellular tissues. It is prepared as follows:—

Make the following solutions separately :

<i>A.</i> Orange G., saturated aqueous solution	120 to 135 parts.
Distilled water	100 ,,
<i>B.</i> Acid fuchsin, saturated aqueous solution	65 ,,
Distilled water	100 ,,
Absolute alcohol	100 ,,
<i>C.</i> Methyl-green, saturated aqueous solution	125 ,,
Distilled water	100 ,,
<i>D.</i> Absolute alcohol	100 ,,
Glycerin	100 ,,

Mix the four solutions slowly and thoroughly. Allow to stand for some weeks before using; then pipette off, as required, the middle layers, without disturbing the sediment.

Stain sections for from fifteen minutes to twelve hours, wash in dilute alcohol, then for one minute in absolute alcohol. Wash thoroughly in xylol and benzol (§ 193), and mount in xylol balsam (§ 199).

Sections, after staining, may be rinsed in a very dilute solution (1-1000) of acetic acid, they must then be very thoroughly washed with weak spirit.

To stain dried blood films use this solution undiluted, but in the case of "wet" films dilute with three or four times its volume of distilled water and stain for from five to eight minutes. Wash quickly in water; then for a few minutes in methylated spirit, dehydrate in absolute alcohol, clear in xylol (§ 193), and mount in Canada balsam (§ 199). Excellent results are thus obtained. The neutrophile granules are stained violet, the eosinophile granules bright red. The nuclei of the polymorpho-

nuclear cells and eosinophile cells take on a greenish-blue colour, those of the lymphocytes a deep blue, and the nuclei of the mononuclear hyaline cells a pale blue. The erythrocytes take on a copper colour, and the nuclei of the hæmatoblasts a very intense blue, darker even than that taken on by the nuclei of the lymphocytes.

149. The original Biondi-Heidenhain stain is useful for staining karyokinetic figures in tissues fixed in corrosive sublimate. The resting nuclei are stained blue-violet, the mitotic figures green.

The best description of this stain is given by Mallory and Wright. Mix *saturated* aqueous solutions of

Orange G.	100 parts.
Acid fuchsin	20 „
Methyl-green	50 „
For staining take of the combined solution .	1 part.
Distilled water	100 parts.

In order to determine whether the proper combination of stains has been obtained, add a few drops of acetic acid, when the solution should become redder. A drop of the solution on filter paper should make a blue spot with green in the centre and orange at the periphery. If a red zone appears outside the orange, then too much acid fuchsin is present.

150. *Victor Bonney's rapid triple stain.*—Prepare the following solutions:—

(1) *Methyl-violet pyronin solution.*

Methyl-violet	0.25 gm.
Pyronin	1.0 „
Aq. dest. ad	100 c.c.

Dissolve and filter.

(2) *Orange acetone.*

To 100 c.c. of acetone add slowly, drop by drop, a 2 per cent. aqueous solution of orange G. heated, cooled, and filtered, stirring the mixture vigorously with a glass rod. When the fluid has attained a pale yellow colour, a faint cloudiness appears, then a flocculent precipitate which presently redissolves as the orange G. is added drop by drop. Immediately this has taken place filter and store in a stoppered bottle. Add the orange G. solution very slowly, otherwise a

precipitate is thrown down. After twenty-four hours a crystalline precipitate appears ; this continues to increase, but the efficacy of the solution is not impaired for some weeks, and then its action may be reinforced by the addition of a few drops of the aqueous solution of orange G.

Fix the section on the slide (§ 98). Stain for two minutes in (1), wash rapidly in water and wipe the slide dry around the section ; flood the slide with (2), a colour-cloud appears ; pour off and flood again with (2) until no more colour comes out ; wash rapidly with pure acetone, taking care not to allow the slide to dry, clear (§ 193) in xylol and mount (§ 199).

If the section be over- or under-stained return it through acetone to water and proceed as before until the requisite tints are obtained.

All chromatic substance is stained by the methyl-violet ; mitotic figures and nucleoli show very distinctly ; and lymphocytes, in which the nucleus is wholly chromatic, are rendered very prominent. Keratin, either of surface epithelium or occurring in cell nests, is also stained violet. The cytoplasm of all cells is stained varying degrees of red by the pyronin, the bodies of plasma cells in particular are vividly stained ; so also are those of epithelial cells, especially when belonging to the deeper layers of squamous epithelium ; the cytoplasm of fixed tissue cells and endothelial cells is less strongly tinted. The connective tissue framework is stained yellow by the orange G., as is also the intercellular substance between the epithelial cells. This stain may be used in routine work instead of hæmatoxylin. It is quite permanent, and may be combined with Weigert's elastic tissue stain (§ 167).

151. *Jenner's* eosin and methylene-blue blood stain gives excellent results. Jenner himself laid special stress on the following points. The bottles that are to hold the reagent should be perfectly clean, dry, and well-stoppered. In one of these a 0.5 solution of Grübler's eosin, yellow shade, soluble in water, is dissolved in absolute methyl alcohol (E. Merck's "for analysis"). In the second a 0.5 per cent. solution of Grübler's medicinal methylene-blue is dissolved in the same kind of methyl alcohol. With 12 c.c. of the former solution mix 10 c.c. of the latter, and keep ready for use in a clean, dry, and well-stoppered drop bottle. Pour this solution on the prepared blood film (§§ 59, 152, and 171), cover at once with a watch-glass to prevent evaporation, and leave for from two to four minutes. Wash films in water until a

faint pink tinge appears. Dry rapidly with blotting paper and mount in Canada balsam (§ 199).

152. To examine the blood for malarial and other protozoal parasites, make a thin cover-glass preparation in the ordinary fashion, and examine at once. In most cases, however, it is necessary to make stained preparations on slides. A thin film is made by drawing or pushing a micro slide from which two corners have been cut off over the drop of blood placed near one end of a slide, altering the contained angle according to the thickness of film required. This leaves a clear space on each side of the film. The film may be stained by any of the following methods.

153. *Leishman's stain* (*Brit. Med. Journ.*, 1901, vol. ii. p. 757)—

Solution A.

Medicinal methylene-blue (Grübler)	1 part.
Distilled water	100 parts.
Sodium carbonate	1.5 part.

Heat to 65° C. for twelve hours, then allow to stand at room temperature for ten days.

Solution B.

Eosin extra B.A. (Grübler)	1 part.
Distilled water	1000 parts.

Solutions A and B āā.

Mix in a large open vessel and allow to stand for from six to twelve hours, stirring from time to time with a glass rod. Filter and wash the precipitate which is thrown down with a large volume of distilled water until the washings are colourless, or only a pale blue tinge remains. Collect the insoluble residue, dry and pulverise.

Make a 0.15 per cent. solution of this powder, which may be obtained from Grübler & Co., Leipzig, in absolute methyl alcohol (Merck's "for analysis"), and transfer to a clean, dry, well-stoppered bottle. Pour 3 or 4 drops of this stain on to the prepared film (blood, bone, marrow, etc.), and move from side to side. After about half a minute add 6 to 8 drops of distilled water, and mix thoroughly by moving the glass slide. Allow to stain for five minutes or, if the film be

thick, for ten. Wash with distilled water, leaving a drop or two on the cover for about a minute. Examine at once or after drying without heat and mounting in xylol balsam (§ 199).

It is sometimes difficult to obtain pure methyl alcohol, and Tulloch (*Journ. Roy. Army Med. Corps*, 1904, vol. iii. p. 166) recommends alkalised spirit made by adding 2 drops of a 10 per cent. solution of potassium bicarbonate to 25 c.c. of methylated spirit. In Leishman's method the blood is fixed by the methyl alcohol of the staining fluid; in Tulloch's method it is first fixed for ten minutes in a mixture of methylated spirit and ether in equal proportions, or in methylated spirit alone for fifteen minutes. The stain may therefore be diluted at once. After staining "the film is washed by dipping it into a vessel of distilled water and moving it to and fro for about thirty seconds. It will be seen, even after this, to have a bluish tinge. It is next washed with dilute acetic acid ($\frac{1}{1500}$), and in a few seconds becomes a bright 'eosin' pink." Rinse in distilled water, dry by blotting, and mount in balsam (§ 199).

In order to utilise this stain for tissues, Leishman (*Journ. Hyg.*, 1904, vol iv. p. 434) recommends that after removing all trace of paraffin by heat, xylol, and alcohol, and washing out the alcohol with distilled water, the section should be blotted, and a drop or two of fresh blood serum placed upon it and allowed to soak into it for five minutes. Remove any excess of serum by blotting, and allow the remainder to dry as a thin film on and around the section. The staining fluid is diluted by adding 3 parts of distilled water to 2 of the stain, and is allowed to act on the tissues for about one to one and a half hours, fresh stain replacing the old, once or twice, during this period. Wash with distilled water, decolorise alternately with 1 : 1500 acetic acid and 1 : 7000 caustic soda, freshly prepared with distilled water, until the required colour contrasts are obtained, this being observed under a low power of the microscope. Blot thoroughly, and use alcohol for dehydration as little as possible, clear in xylol (§ 193), and mount in balsam (§ 199).

154. Ross has devised a method of finding parasites in the blood which greatly facilitates diagnosis in such conditions as intermittent fever. He takes, on a slide or cover glass, a *large* drop of blood amounting to as much as 20 cubic millimetres; this is spread out *in a thick film* by means of a needle or lancet. Dry, preferably not over

a flame. When thoroughly dry run from a glass rod enough aqueous eosin solution (Romanowsky) to cover the film. At the end of about a quarter of an hour most of the hæmoglobin from the mass of corpuscles has been dissolved out by the water of the eosin solution, and nothing is left but the stromata of the red blood corpuscles, the leucocytes, the blood platelets, and the parasites. Wash with a very gentle current of water (do not wash away the "unfixed" film) to get rid of excess of eosin. Now add a few drops of methylene-blue (Romanowsky), and stain for a few seconds only. (Don't stain too deeply.) Again wash gently in water, dry and mount in xylol balsam (§ 199). The parasites, which are, of course, much more numerous in such a specimen than in an ordinary blood film, are seen as blue bodies or rings with red nuclei. For diagnostic purposes Ross also uses de hæmaglobinised blood films unstained, in which the pigmented parasites may be readily seen.

155. J. Homer Wright uses the following stain for malarial parasites and Leishman-Donovan bodies:—

Sodium bicarbonate	.	0.5	gram.	
Distilled water	.	100	c.c.	Dissolve and add
Methylene-blue	.	1	gram.	

Steam this mixture in an ordinary *steam steriliser* for one hour. Cool and pour into a large vessel and add to it, stirring or shaking meanwhile, 500 c.c. of a 1-1000 aqueous solution of eosin (Grübler, yellowish water-soluble). In the mixture thus formed a fine blackish precipitate will be visible in suspension, and on the surface a scum with a yellowish metallic lustre. Filter the mixture; do not wash but allow the filtrate to dry thoroughly; dissolve 0.5 gram. of filtrate in 200 c.c. pure methyl alcohol. Either the dry precipitate or the alcoholic solution will keep for an indefinite length of time; evaporation of the alcohol should be prevented even during the process of staining, otherwise a precipitate may be thrown down on the specimen. Cover-glass preparations after being air dried should be placed in pure methyl alcohol for two or three minutes. Then without allowing the film to dry cover with the stain, at the end of a minute add water "drop by drop until a delicate scum with iridescent metallic lustre becomes visible on the surface," then *stop the dilution*. "If the staining fluid has been properly prepared, this scum will form before the fluid has

been diluted enough to be transparent; the diluted fluid is to remain on the preparation for three minutes." Wash in distilled water for about a minute until the nuclei of the cells in the better spread portions of the preparation appear well differentiated under the low power of the microscope, and until any red blood corpuscles present have a yellowish or pinkish colour. Dry and mount in balsam (§ 199). "The nuclei of cells should have a blue or deep lilac colour and red blood corpuscles a pink or orange colour." The cytoplasm of the polymorpho-nuclear leucocytes should show lilac coloured granules, and the cytoplasm of the lymphocytes should have a robin's egg blue colour. The Leishman-Donovan bodies take on the robin's egg blue, the central portion remaining unstained. Within most of these are the lilac stained bodies, the larger one not quite so deeply stained as the smaller, sometimes rod-shaped body. These bodies are usually situated near the periphery of the blue stained masses.

The bodies of malarial parasites are stained blue; the colour of the chromatin varies from a lilac, through varying shades of red, to almost black. In the young forms of the tertian and æstivo-autumnal parasites the chromatin appears as a spherical, very dark, body, while in the older forms of the tertian parasite it has a more lilac or purplish-blue colour, and may appear in the form of a reticulum. In the intermediate forms the colour of the chromatin may present great variations between these extremes. In the young parasite the spherical nucleus is dark red, whilst the surrounding cytoplasm is seen as a distinct blue ring.

The granules found in red blood corpuscles in which the malarial parasite is present can be brought out by staining for a longer period—at least five minutes; this to be followed by a less complete washing and differentiation with the distilled water.

156. *The Nocht modification of the "Romanowsky" stain.*

No. 1.—Polychrome methylene-blue (Grübler's); is neutralised, exactly, with 3 per cent. acetic acid; this requires about 5 drops of the acid solution to 1 oz. of blue.

No. 2.—1 per cent. aqueous solution Ehrlich's methylene-blue, prepared by dissolving by slight heat. Allow to stand for at least one week.

No. 3.—1 per cent. aqueous solution Grübler's eosin.

To 10 c.c. of distilled water, add 4 drops of No. 3 solution, 3 drops of No. 1, and 2 drops of No. 2, in the order named, mixing after each addition. Fix films in alcohol, dry without heat. Stain face downwards for from one to two hours. Wash in water and allow to dry or clear (§ 193), and mount in xylol balsam (§ 199).

157. Giemsa's modification of Romanowsky's stain.—Giemsa uses a solution of his stain Azur II., which is a mixture in equal parts of pure methylene azur "chlorhydrate" and methylene-blue "chlorhydrate." The stain, which may be obtained ready made from Grübler of Leipzig under the name of "Giemsa'sche Lösung für die Romanowsky Färbung," is prepared as follows:—

Azur II.-eosin compound	3 grms.
Azur II.	0.8 gm.

Mixed and well dried in the desiccator over sulphuric acid, are *very finely pulverised*, then passed through a fine meshed silk sieve and dissolved at 60° C. in Merck's glycerin, 250 grms., the mixture being well shaken. 250 grms. of methyl alcohol (Kahlbaum I.), which has been previously heated to 60° C. is then added. This mixture, after being well shaken, is allowed to stand for twenty-four hours, and is then filtered. The solution is now ready for use, and should be kept in a yellow glass bottle.

To 1 c.c. of ammonia-free distilled water add 1 drop of this stain. Stain from a quarter to three-quarters of an hour. Wash in running water, blot, dry, and mount in Canada balsam (§ 199).

Greater dilution of the Giemsa solution and longer exposure to the action of this dilute fluid often give excellent results.

The best fixatives for blood to be stained by Giemsa's solution are perosmic acid vapour for three seconds; 10 per cent. formaldehyde in absolute alcohol for three seconds; methylic alcohol for three minutes; or ethylic absolute alcohol for ten minutes. Scott's method may also be used (§ 59). Be careful to use only ammonia-free distilled water and methyl alcohol in rinsing out bottles, watch-glasses, etc.

For general purposes this stain may be used in the following manner:—

For films of secretions or scrapings, either the dry or the wet method may be adopted. Prepare and fix the film on a slide; pour on a few drops of the strong stain, and allow it to stand for a single

minute; then add two or three times the amount of distilled water, allowing the stain and the water to mix on the film. After leaving for fifteen minutes, wash off the stain with distilled water, and allow the preparation to remain in some freshly distilled water for ten minutes. If you are staining a dry fixed film, dry in the air and mount in Canada balsam. If a wet fixed film, blot with white filter paper and dehydrate in acid alcohol. Clear in xylol (§ 193) and mount in Canada balsam (§ 199).

From sections cut in paraffin and fixed on slides by the warm water method, dissolve out the paraffin with xylol and wash in spirit. Cover the section with a small pool of the stain, which is allowed to act for one or two minutes; then add distilled water (equal parts) to the stain; allow to mix thoroughly on the section and leave for fifteen to thirty minutes. Wash in water. To remove the water, blot the section with a piece of clean white filter paper, then rapidly dehydrate with acidulated alcohol (4 drops of glacial acetic acid to 1 oz. of absolute alcohol), transfer quickly to xylol (§ 193), and mount in Canada balsam (§ 199).

Leishman's stain (§ 153) used in the same way gives excellent results.

158. Levaditi's method for staining spirilla and trypanosomes in tissues.

—(1) Fix fragments of the tissue, not more than 1 mm. thick, in 10 per cent. formol solution for twenty-four hours. Rinse in distilled water and harden in 96 per cent. alcohol for twenty-four hours. Then wash in distilled water for some minutes, *i.e.* until the pieces fall to the bottom of the vessel, and transfer to a solution of nitrate of silver of a strength of from 1.5 to 3 per cent. (3 per cent. is preferable when the tissues have been obtained from the living patient). This impregnation should be carried on at 38° C. for from three to five days, according to the nature of the tissue. "Reduce" the silver in the following solution:—

Pyrogallie acid	2-4 per cent.
Formol	5 c.c.
Aq. dest.	100 ,,

Allow this solution to act on the tissues for from twenty-four to forty-eight hours at room temperature. Again wash in distilled water; then dehydrate with alcohol, clear with xylol and cedar oil (§ 193), and embed in paraffin (§ 94). The sections should not be more than 5 μ thick.

Stain sections (1) with Giemsa's stain (§ 157) for some minutes : wash in water differentiated with absolute alcohol to which have been added some drops of clove oil ; clear with oil of bergamot and xylol (§ 193) and mount in xylol balsam (§ 199) ; or

(2) Stain sections with a concentrated solution of toluidin-blue (§ 115) ; differentiate with alcohol to which have been added several drops of Unna's glycerin ether solution. Clear with oil of bergamot and xylol (§ 193), and mount in xylol balsam (§ 199).

Spirochaetes come out black, nuclei of cells blue, and the formed material of the connective tissue and muscles green.

159. Ehrlich's neutral red reaction in intracellular digestion offers a method to which, up to the present, far too little attention has been paid.

To demonstrate the process of phagocytosis by the round cells of the frog, make an incision in the skin of the frog just above the dorsal lymph sac, and introduce into the sac a large loopful of a young and vigorous culture of *B. anthracis*. Two or 3 drops of a 1 per cent. solution of neutral red may be introduced at the same time. If this be not added at the time, the neutral red should be injected into the sac fifteen minutes before the lymph is withdrawn, which should be examined three, and on to forty-eight hours, after the introduction of the bacilli. The advantage of placing the neutral red in the lymph sac some time before the lymph is to be first examined is that under these conditions few crystals are formed.

The functional activity of these cells depends very largely upon the time of the year, the cellular digestion going on most rapidly in the summer months, whilst in winter phagocytosis appears to come almost to a standstill. In summer the round cells of the frogs' lymph very quickly become crammed with anthrax bacilli, stained in tints varying from a deep brick-red to a faint pink, the brick-red stained organisms usually showing signs of degeneration. Bacilli may sometimes be observed which are only partially taken into the phagocyte ; these are specially interesting because they show neutral red staining only where they have been acted upon by the acid ferment of the cell, the portion outside the cell being quite unstained, as are also all the free organisms.

This reaction can also be obtained with human leucocytes and other bacteria maintained *in vitro* at incubator temperature—a variation of the usual opsonin technique. The phagocytic cells may afterwards

be stained with either Jenner's (§ 151), Leishman's (§ 153), or Homer Wright's (§ 155) stain. This method may also be used for the purpose of demonstrating the acid digestion of red blood cells carried on by intra-corpuscular parasites such as *Piroplasma canis*. Defibrinated or citrated blood is mixed in a capillary pipette with about an equal quantity of 1 per cent. aqueous solution of neutral red, the pipette is then sealed and placed in the incubator at 37° C. for from fifteen to thirty minutes (Baldrey and Mitchell, *Journ. Tropical Vet. Science*, Calcutta, 1907, vol. ii. p. 169).

On examining films of the blood from these pipettes it will be seen that the parasite is the source of the acid ferment (acid cytase), giving the characteristic brick-red reaction in the more vigorous and actively digesting parasites in the red cell. Free-floating parasites generally give less reaction.

As a control the parasites may be killed by the addition of a weak antiseptic. If the blood is then mixed with neutral red and incubated as above, only a pale yellow, never a red, reaction is obtained.

160. Unna's stain.—In certain inflammatory processes Unna has described cells the protoplasm of which stains somewhat deeply in alkaline methylene-blue solutions. After hardening in absolute alcohol, sections are stained in polychrome methylene-blue for from five minutes to a quarter of an hour; they are then washed in water, decolorised and dehydrated in a $\frac{1}{4}$ per cent. alcoholic solution of neutral orcein (this takes about fifteen minutes), after which they are completely dehydrated with absolute alcohol, cleared with xylol (§ 193), and mounted in xylol balsam (§ 199). Unna also uses polychrome methylene-blue solution to which a little alum has been added in order to stain the protoplasmic granules of "mast" cells in tissues hardened in alcohol. He leaves the sections in this solution for from three to twelve hours, washes them in water, dehydrates in absolute alcohol, clears in bergamot oil, and mounts in balsam. The nuclei are stained blue, the "protoplasmic granules" and the "mast" cells red.

161. Pappenheim's stain.—Pappenheim, who worked with Unna, stains sections, in which plasma cells and mast cells are to be looked for, for from two to five minutes in a fairly concentrated watery solution of methyl-green and pyronin, which he prepares fresh each time that it is used, in the following fashion. On the point of a penknife take

1 to 2 parts of methylene-green and 2 to 4 parts of pyronin; this is placed in a test-tube which is filled with water (up to one-half) until the solution has a distinct reddish-violet colour. A small quantity of this fluid dropped on a filter paper gives a bright green peripheral ring, the margin of which is lost in a dark violet-red centre. Wash the section in water for a few moments, then differentiate with 2 to 3 parts of resorcin measured in the same way into a quarter of a test-tubeful of absolute alcohol (before this washing in the alcoholic resorcin Arthur Eastwood recommends a preliminary washing with a saturated watery solution of resorcin); dehydrate rapidly in alcohol, clear with one of the ethereal oils (§ 193), and mount in balsam (§ 199). Cover-glass preparations may be stained in the same way.

By this stain the nuclei of the polymorpho-nuclear leucocytes are stained of a transparent green, cell plasma and neutrophile or ϵ granules remaining unstained. The oxyphile or α granules appear as unstained vacuoles in a reddish cytoplasm, the basophile or γ granules appearing as a beautiful orange or scarlet red; the nuclei of the mononuclear lymphocytes and leucocytes appear in various gradations from reddish-blue to bluish-red, or from a dull violet to lilac; the basophile cytoplasm of lymphocytes and plasma cells is stained bright purplish-red.

162. Unna's modification of Pappenheim's stain is useful for the study of the cellular elements in inflammation.

It is specially useful for preparations fixed in corrosive sublimate, thoroughly washed and then treated with Lugol's iodine solution.

1 per cent. pyronin, watery solution . . .	5 drops.
1 per cent. methyl-green, watery solution . . .	15 „
1 per cent. resorcin, watery solution . . .	10 „

Distilled water must always be used as the solvent for these stains.

Mix as required and filter on to the sections, allowing the stain to act for ten minutes or longer. Wash in water. Dehydrate rapidly in methylated spirit, and then quickly in absolute alcohol, clear in xylol (§ 193), and mount in Canada balsam (§ 199). See Fig. 20, p. 202.

163. *Unna's slow differentiating method.*—Stain in polychrome methylene-blue solution (Grübler) for two minutes, rinse well in water, and decolorise for from one to two minutes, according to the thickness of the section, in glycerin-ether mixture (Grübler), 1 part to 4 parts

of water, rinse thoroughly in water from two to five minutes, dehydrate with absolute alcohol, clear in bergamot oil (§ 193), and mount in xylol balsam (§ 199).

METHODS OF STAINING SECRETION—AND OTHER GRANULES

164. *Beckton's modification of the Altmann-Schridde staining method for demonstrating granules in "mast" cells, lymphocytes, and other cells.*—Fix and harden (§ 64*b*) the tissue and prepare the following staining solutions:—

Solution 1.

Aniline oil	5 c.c.
Aq. dest.	100 „
Acid fuchsin	20 grms.

Mix the anilin oil with the water in a flask, shaking vigorously at intervals, and filter into a graduated measure until 100 c.c. of filtrate has run through; the excess of anilin oil remains in the filter. To the filtrate add the 20 grms. of acid fuchsin, shaking well, and filter.

Solution 2.

Concentrated solution of picric acid in alcohol	50 c.c.
Aq. dest.	100 „

Mix.

Sections not more than 2 to 5 μ in thickness are stained on the slide placed vertically in a large volume of solution 1 for from ten to thirty minutes; they are then washed in solution 2 or with picric acid alcohol:—

A saturated picric acid solution in absolute alcohol 1 vol.

Absolute alcohol, 20 per cent. solution in water 7 vols.

Allow the slide to remain, in a vertical position, for from five to fifteen minutes. The advantage of this over the Altmann and Schridde method is that the staining and differentiation are both carried on at the room temperature.

The "granules" are stained bright red, are uniform in tint, and are still highly refractile. They stand out distinctly from a pale yellow or greyish-yellow background—the cell protoplasm. Sections so prepared may be decolorised and re-stained in other reagents,—a very great

advantage where a close study of the granules and cell structure is to be made.

165. *Richard Muir's method of differential staining of granules in tissue cells.*—Fix the tissue in a 2·5 per cent. watery solution of formalin (Schering's) for from twelve to twenty-four hours. Wash in running water for ten minutes and transfer to methylated spirit, and allow it to remain there for three or four days. Embed in paraffin (§ 94). Cut sections and fix on glass slides (§ 98), remove the paraffin with benzole and the benzole with methylated spirit. Flood the section with a saturated solution (excess of crystals) of alcoholic eosin crystals dissolved in equal parts of absolute alcohol and water. Heat the flooded section gently over a Bunsen flame, and allow the evaporating alcohol to ignite. Blow out the flame at once. Repeat this several times until the alcohol has all been driven off. When there is no further ignition, the staining with eosin is complete. The watery solution of eosin, which should still remain but in which there should be no crystals, is washed away with running water. Fix the eosin in the section by filtering on to it a few drops of a saturated watery solution of potash alum, which at the end of three minutes is washed away with running water. Decolorise with methylated spirit to which strong ammonia has been added in the proportion of one *öse*-ful to each ounce, until the specimen retains only a faint red tinge. Wash thoroughly in water, dehydrate in absolute alcohol, clear in benzole (§ 193), and mount in Canada balsam (§ 199).

By this method eosinophile granules may be demonstrated in active cells and in certain pathogenic conditions, such as cloudy swelling.

The above method may be combined with Heidenhain's iron alum stain.

The section after being lightly stained with hæmatoxylin solution (§ 110 (b)) is decolorised with the iron alum solution, the process being watched under a low power lens until only the nuclear wall, the chromatin "net knots," and the nucleoli, show any hæmatoxylin staining. Wash thoroughly, first in water and then with methylated spirit. Now stain with eosin and methylene-blue as above described. See also §§ 133*a* and 151–159.

166. Borrel's stain was introduced in connection with the staining of cancer preparations, but has been used by Laveran and Mesnil for the staining of trypanosomata.

A. Dissolve a few crystals of nitrate of silver in about 60 c.c. of

distilled water. On adding an equal bulk of caustic soda solution a black precipitate of silver oxide is thrown down. Wash with water, on a filter, several times, in order to remove excess of soda, and then pour over the silver oxide a saturated solution of medicinal methylene-blue (Höchst), and allow to stand for fifteen days, shaking several times daily.

B. Prepare a 1 per cent. aqueous solution of eosin (Höchst, water soluble). Prepare films or sections before the following mixture is made. Films to be stained for trypanosomata should be dried and placed at once into absolute alcohol for five minutes and then film downwards in

<i>C.</i> Solution A	1 part.
Solution B	4 parts.
Distilled water	6 „

This must be prepared at the moment it is to be used. Leave for fifteen or twenty minutes. Wash well in water, then transfer to 5 per cent. tannic acid solution, leave for ten minutes, wash again in plenty of water and dry. If any precipitate is deposited on the film, wash in plenty of water and brush lightly with a camel's-hair pencil, clear with clove oil (§ 193); wash with xylol and mount in xylol balsam (§ 199). By this method the outlines of the organisms are well preserved, the protoplasm stains a pale blue, the nucleus a bright reddish-violet, the flagellum either a bright red or the same colour as the nucleus.

167. *Weigert's elastic fibre stain—*

<i>Solution A.</i> Fuchsin soluble in water . . .	1 part.
Distilled water	100 parts.
<i>Solution B.</i> Resorcin	2 „
Distilled water	100 „

Mix, boil, and to the boiling mixture add liquor ferri perchloridi, 25 parts; boil for five minutes, stirring all the time; cool and filter. Place the filter paper along with the residuum in 200 parts of 94 per cent. alcohol, tear up the filter paper, boil and remove the fragments, squeezing out as much of the fluid as possible from the paper; cool and filter. Add 90 per cent. alcohol to make up to 200 parts. Add 4 parts hydrochloric acid. Allow to stand for a couple of days.

Stain sections with lithium carmine (§ 107), then in the above

solution for from ten to twenty minutes, wash in dilute alcohol, dehydrate, clear in xylol (§ 193), mount in balsam (§ 199). Hæmatein and van Gieson's stain (§ 103) may also be used, along with this elastic tissue stain, the staining taking place in the following order: hæmatein, Weigert's stain, picro-fuchsin. The elastic fibres are stained blue, the other tissues stain as usual.

168. *Unna's orcein method* also gives a very reliable and delicate stain with elastic fibres.

Orcein (Grübler)	1 part.
Hydrochloric acid	1 „
Absolute alcohol	100 parts.

The sections immersed in plenty of the above solution, in a covered capsule, are placed in an incubator for ten to fifteen minutes, or are kept for twelve hours at the room temperature. Wash thoroughly in 70 per cent. alcohol, then in water, to remove acid and excess of stain; dehydrate, clear (§ 193), and mount in balsam (§ 199). Unna's polychrome methylene-blue solution (§ 116) is recommended as a contrast stain, which is applied before the specimen is dehydrated.

168a. An excellent stain for connective tissue fibrillæ and reticulum has been devised by Mallory.

Fix and harden (§§ 61 and 63), embed (§ 94).

Stain sections in a 1 to 10 per cent. aqueous solution of acid fuchsin at least five minutes. Transfer for twenty minutes or longer to

Anilin-blue soluble in water (Grübler)	0.5
Orange G (Grübler)	2.0
Phosphomolybdic acid, 1 per cent. aqueous solution	100.0

Wash and dehydrate in several changes of 95 per cent. alcohol, clear in xylol or in oleum origani cretici (§ 193), and mount (§ 199).

“The fibrillæ and reticulum of connective tissue, amyloid, mucus, and certain other hyaline substances stain blue; nuclei, protoplasm fibroglia fibrils, axis cylinders, neuroglia fibres, and fibrin red; red blood corpuscles and myelin-sheaths yellow; elastic fibres pale pink or yellow.”

To bring out the connective tissue as sharply as possible, omit the preliminary staining with acid fuchsin. The blue fibrillæ and reticulum then stand out more prominently from the yellow background.

169. *Fibrin* is stained yellow by most stains containing picric acid, but it is sometimes desirable to bring the fibrin into special prominence, especially in acute inflammations. For this purpose Weigert has devised the following method: Stain the sections in alum carmine (§ 106) for from one to twelve hours; then wash and stain in carbol gentian-violet (§ 119) for from five to twenty minutes. After removing the excess of stain with blotting paper or by means of normal salt solution, treat with dilute Lugol's solution (§ 42) for from a half to one minute; wash this off with water or blot until the section is quite dry. Decolorise with Weigert's clearing solution (anilin 2 parts, xylol 1 part); wash well in xylol (§ 193) and mount in balsam (§ 199). Specimens hardened in the chrome salts solutions should first be soaked for several hours in a 5 per cent. aqueous solution of oxalic acid.

170. *Lorrain Smith's method for staining fat with anilin dyes.*—Stain a frozen section in a watery solution of one of the basic anilin dyes (methyl-violet or basic fuchsin). Wash off the superfluous stain with water, and expose to the air in a thin layer of Farrants's solution. A trace of sulphurous acid added to the solution of the dye ensures more perfect staining of the fat. If nuclear stains be added—Mayer's carmalum to methyl-violet, or acid hæmatoxylin to basic fuchsin—good definition of the nuclei is obtained along with the sharp staining of the fat. When the latter combination is used, the section before being mounted in Farrants's solution (§ 195) should be washed in a dilute solution of lithium carbonate in order to define the blue of the nuclei.

Lorrain Smith also points out that the fat of frozen sections of tissues hardened in formalin stains readily in a watery solution of Nile-blue sulphate. This appears to be a mixture of substances of such a nature that certain globules of fat are coloured red, others blue, according to their composition. The globules met with in fatty degeneration of the heart often stain red. The same is true of the fat in liver cells, though, if the sections of a fatty liver are exposed to the stain for a few hours in the incubator at 37° C., certain of the fat globules assume a blue or purple colour. This stain is recommended for the study of the fat

necroses of the pancreas and of the degenerated medullated fibres in nerve tissues.

MICROSCOPIC EXAMINATION OF TISSUES AND FLUIDS CONTAINING BACTERIA

171. In connection with the manipulation of sections and fluids in which the presence of bacteria is suspected, it must be remembered that the greatest cleanliness is requisite — not only apparent but absolute; and to obtain this absolute cleanliness the apparent must first be attended-to. No spot or blemish of any kind should be seen on any of the instruments used; the point of the knife or the platinum needle which conveys the fluid must be carefully polished; the cover-glasses and slides thoroughly washed with acid or with van Ermengem's fluid (§ 35*a*) and then with alcohol and distilled water; the watch-glasses and other utensils should be treated in a similar manner, and the whole carefully heated to a temperature above that at which organisms can exist—150° C. This is most readily done by passing them carefully through the flame of a spirit lamp, though it is very convenient to have a hot-air chamber in which the various utensils may be sterilised and kept when not in use.

The staining of bacteria is now so quickly and easily carried out, that except in the case of a "hanging drop" preparation it is seldom considered necessary to examine these organisms unstained. Here it is necessary to give a few of the simpler methods only; for special bacteriological investigation the student is referred to works on practical bacteriology. Weigert and Koch introduced the methods of staining either the parasites alone, or the parasites and the nuclei, with a watery solution of some of the anilin colouring reagents. (It will be well for those who are "red" colour blind to use Gram's method, and to avoid the red stains.) Sections or cover-glass preparations are immersed, face downwards, in a saturated watery solution of gentian-violet, methylanilin-violet (ten minutes), methyl-blue (thirty minutes), or Bismarck brown (twenty-four hours), in which they must be allowed to remain until they are deeply stained; the time required for staining varies with the temperature and the reagent used. Wherever great intensity or rapid staining is required, the fluid may be warmed in a watch-glass. When the colour is deep enough the sections are washed for a few seconds in distilled water, then in weak acetic acid, and again in

distilled water. In many cases it is better to remove the staining fluid by means of blotting paper instead of with water or alcohol, etc., the preparation after thorough drying being embedded at once in Canada balsam (§ 199). If the nuclei are to be left tinted, the section is passed *rapidly* through alcohol and clove oil (§ 193), and mounted at once in xylol balsam (§ 199). Where, however, preparations are over-stained, with methylene-blue, say, they may be partially decolorised and differentiated with water to which a few drops of acetic acid have been added. In place of the watery solutions, a saturated alcoholic solution of almost any of the germ-tinting anilin colours may be made up in considerable quantity, and diluted as required with about ten times its bulk of distilled water. This stains more rapidly, and is exceedingly useful for the demonstration of the presence of micrococci. All the staining reagents should be carefully protected from both dust and light, *and should always be filtered* before they are used. If the nuclei are to remain unstained, and the tissues are to be cleared up as much as possible, the section is first stained as above, washed in distilled water, and then transferred to a 5 per cent. solution of carbonate of potash, by which the colouring matter is discharged from all the tissues of the host, but is left in the bacilli or micrococci. The section is then mounted in either Canada balsam (§ 199), Farrants's solution (§ 195), or glycerin (§ 194). This method is especially valuable for the demonstration and enumeration of bacilli contained within vessels or in thick sections, as in intestinal mycosis, where the anthrax bacilli are to be observed *in situ* in the capillary vessels of the intestinal villi. As a contrast or counter stain Weigert recommends lithium carmine. For pus, blood, and other fluids the so-called dry method is, for most purposes, perhaps more convenient. The fluid to be stained is smeared on a cover-glass in a very thin layer, which is best obtained by pressing two cover-glasses together, and then "sliding" them apart. The thin film on these glasses is slowly dried, either at the ordinary temperature or by holding it at some distance away from the spirit lamp or gas flame; the glass is then held with a pair of forceps, and passed rapidly through the flame—the smeared surface away from the flame—until the whole of the albumin in the stratum is coagulated. In doing this the glass should first be held at some distance from the flame, and then passed thrice rapidly through it, great care being taken not to *scorch* the film. It may be stained at once, or, if carefully protected from moisture and dust, it may be left

for future treatment. Stain with one of the above fluids, floating the cover-glass, smeared side down, on the surface of the fluid; wash in distilled water and dry carefully, and mount at once in Canada balsam (§ 199). It may be mentioned that although Canada balsam is most frequently used for preserving these bacilli, Farrants's solution (§ 195) and glycerin (§ 194) are both excellently adapted for this purpose, especially in the case of sections of tissues and of tubercle bacilli.

172. One of the best general stains for bacteriological work is *Kühne's methylene-blue* solution. 1.5 grm. of methylene-blue is dissolved in 10 c.c. of absolute alcohol and 100 c.c. of a 1 to 20 watery solution of carbolic acid, added gradually. Specimens are stained in this fluid for from five minutes to two hours, although sections may be left in it for a whole day without becoming over-stained. They are then carefully washed in distilled water, then with acidulated water, made by adding a couple of drops of hydrochloric acid to 100 c.c. of water. As soon as the sections become a pale blue colour they are transferred to a solution of lithium water—1 part of lithium carbonate to 20 of water; they are then thoroughly washed in pure water, dehydrated by means of absolute alcohol in which a little methylene-blue has been dissolved, placed in anilin oil, which may or may not contain a small portion of methylene-blue in solution, and rinsed in pure anilin oil. After this treatment they are transferred to terebene, in which they are left for about a couple of minutes. They are then washed in two lots of pure xylol and mounted in Canada balsam (§ 199). Almost any micro-organism may be stained by this method, even the glanders bacillus coming out fairly distinctly.

173. *Gram's method*.—The sections to be stained by this method should be kept in absolute alcohol, from which they are transferred to the ordinary gentian-violet and anilin water or carbolic acid water solution (Weigert's or Ehrlich's) (§§ 118, 119), the latter, however, is not so reliable, and left for from one to three minutes (tubercle bacilli should be left for from twelve to twenty-four hours); wash for two or three minutes in alcohol, and then in Lugol's solution (§ 42), until the dark blue-violet is replaced by a dark purple-red. Wash once or twice in alcohol, until most of the colour has

disappeared; then clear up in oil of cloves, until the whole of the colour is washed out from the sections. Mount in balsam (§ 199). The nuclei and tissues are stained yellow, and the micro-organisms, if present, are deep blue or almost black. After the bleaching process, the nuclei may be stained with eosin, vesuvin, or Bismarck brown; the sections are then washed in alcohol, and mounted in balsam (§ 199), glycerin (§ 194), or glycerin jelly (§ 197). Cover-glasses, with thin films of sputum, etc., are treated in exactly the same manner.

174. *Kühne's modification of Gram's method* is perhaps superior to the original. He stains with a 2 per cent. solution of gentian-violet in dilute (50 per cent.) alcohol, to which has been added one-half of its bulk of a 1 per cent. watery solution of ammonium carbonate, or with a similar solution of Victoria-blue, without the ammonium carbonate, for about five or ten minutes. The preparations are then rinsed in water, and are placed in Lugol's iodine solution (§ 42) (2 grms. iodine, 4 grms. iodide of potassium, and 100 c.c. distilled water) for two or three minutes; they are then washed in water, dehydrated with fluorescein alcohol, which is prepared by dissolving 1 gram. of yellow fluorescein in 50 c.c. of absolute alcohol, the part undissolved being allowed to settle at the bottom, the supernatant part only being used. Keep the bottle filled with alcohol until the whole of the fluorescein is dissolved. The section is washed in pure alcohol, then with anilin oil, and mounted in xylol balsam (§ 199).

175. *Davalos-Ziehl solution*.—Davalos recommends a modification of Ziehl's carbol-fuchsin solution as a universal staining fluid for micro-organisms—

Take of basic fuchsin	.	.	.	0·25	part.
Alcohol	.	.	.	10·0	parts.
Cryst. carbolic acid	.	.	.	5·0	„
Water	.	.	.	100·0	„ Filter.

Cover-glass preparations are floated, face downwards, on this solution for one or two minutes. They are then rinsed in water, “blotted” and mounted in xylol balsam (§ 199).

176. As a "capsule" stain Welch's method gives good results. The cover-glass is immersed in glacial acetic acid for a few seconds; this is drained off and the specimen is stained in anilin water gentian-violet (§ 118); it is then washed in a 2 per cent. common salt solution in which it may be examined, or it may be "blotted," allowed to dry, and mounted in balsam (§ 199).

For differential staining of the capsules of bacteria, Richard Muir has made a slight modification of this stain, by which he obtains more constant and better results.

The films or sections of tissues should be thin. Stain for from thirty to sixty seconds in Ziehl-Neelsen's carbol-fuchsin solution, heating gently over a Bunsen flame; wash in water and filter on to the specimen the following mixture:—

Watery solution of tannic acid, 20 per cent.	. 2 c.c.
Saturated watery solution of mercuric chloride	2 "
" " " potash alum	. 5 "

Allow the mixture to act on the film or section for from two to five minutes; differentiate in methylated spirit; wash in water; stain in saturated watery solution of methylene-blue for one minute; again wash in water; dehydrate in absolute alcohol; clear in xylol (§ 193), and mount in Canada balsam (§ 199).

177. Use Möller's method for the staining of spores. Stain with heated carbol-fuchsin (§ 120), decolorising in acid alcohol and counter-staining with methylene-blue (§ 115). The spores are red, the remainder of the bacteria blue. The Ziehl-Neelsen method (§ 183) may be used for the same purpose, great care being taken not to leave the cover-glass preparation too long in the acid.

178. *To demonstrate flagella on bacilli (Loeffler's modified method).*—From a young surface culture, grown on agar-agar, make a hanging-drop specimen and examine it under the microscope. If the bacteria are motile, a drop of the culture is then diluted about one hundred times by means of distilled water. A drop of the diluted fluid is placed on a cover-glass, over which *it is allowed to run in various directions*; it is then dried in the open air or in a warm room at a temperature of 40° C., and *gently* heated by passing three times through a flame, the glass being held between the fingers to guard against

overheating; the bacilli are then mordanted in a solution made up as follows:—

Tannic acid solution	20 parts.
Water	100 „
Cold saturated solution of sulphate of iron	5 „
Saturated aqueous or alcoholic solution of fuchsin or gentian-violet	1 part.

This mordant is filtered on to the cover-glass, where it is left to act for from one-half to one minute. Wash carefully with water to remove the mordant, dry and then stain with a freshly prepared and filtered solution of anilin-water gentian-violet (§ 118), or anilin-water fuchsin. Heat *gently* until steam arises from the stain, wash with water, dry quickly, and mount in xylol balsam (§ 199). In order to be sure of obtaining good results, avoid all manipulation of the emulsion, and heat as little as possible.

Another modification is the following. Cover the film prepared as above with the following mordant for one minute:—

Tannin dissolved in 8 c.c. hot water	2 grms.
Cold saturated aqueous solution of sulphate of iron	5 c.c.
Concentrated alcoholic solution of fuchsin	1 „

Wash and then dry the specimen and filter on to it the anilin-water gentian-violet solution. Heat over a flame until steam arises, and allow to remain for one minute longer. Wash and mount in xylol balsam (§ 199).

179. *Richard Muir's modification of Pitfield's method for staining flagella.*—Clean the cover-glasses thoroughly (§ 35a).

(a) *The Mordant*

Tannic acid, 10 per cent. watery solution (filter)	10 c.c.
Corrosive sublimate, saturated watery solution	5 „
Alum	5 „
Ziehl-Neelsen's carbol-fuchsin stain	5 „

Mix thoroughly and centrifugalise (if a centrifuge is not available,

the mixture may simply be allowed to stand over night). A thick deposit will be found at the bottom of the tubes or vessel. Remove the supernatant clear-coloured fluid with a pipette, and transfer to a clean bottle.

This mordant will keep good for two or three weeks.

(b) *The stain* must be prepared every two or three days.

Alum, saturated watery solution (filter) . . . 10 c.c.

Gentian-violet, saturated alcoholic solution . . . 2 „

This stain may also be used in the mordant in place of the carbol-fuchsin stain.

On the centre of a cover-glass, with a straight platinum needle, place a very small drop of pure distilled water and transfer to it a very minute portion of an agar surface culture of the organism to be examined, spread out carefully with the needle and allow to dry in the air.

Flood the cover-glass with the mordant (a), heat gently over a flame until steam rises, and continue the heating for about one minute; wash well in a stream of gently running water for about two minutes, dry carefully over a flame, and then pour on some of the stain (b). Again "steam" gently over a flame for one minute, and as before wash well in running water for a couple of minutes. If black-stained preparations are preferred, treat with Gram's iodine fixing solution (§ 173) for one minute; dry over a flame, and finally mount in Canada balsam (§ 199).

This method is simpler than van Ermengem's silver method, and as very little precipitate forms on the film, the organisms and their flagella appear to retain their normal proportions. It is more of a true stain than the silver method, which gives a deposit. It is extremely valuable in the study of the shedding of the flagella in spore-bearing bacilli, and in old cultures it brings out the relation of the flagella to the bacilli and the sheaths, and the degenerative changes which they undergo.

180. *Bowhill's method of staining flagella and bacteria, simultaneously, with orcein.*—

1. A suspension of a small quantity of material (in which the bacilli have previously been observed to be motile), taken from the

surface of a young agar culture, is made in boiled and cooled distilled water in a test-tube.

2. The tube is left undisturbed for five minutes, and then 1 drop of the bacterial suspension is air-dried on a clean cover-glass.

3. Fix in the flame, holding the specimen between the fingers to prevent excessive heating.

4. Pour some of the following solution into a watch-glass, float the cover-glass, film side downwards, on the surface of the solution, and heat gently—do not boil—leaving the specimen in a mixture of the following solutions for ten or fifteen minutes:—

(a) Saturated alcoholic solution of orcein (this solution possesses greater staining powers if allowed to stand ten days before it is used).

(b) 20 per cent. solution of tannic acid in water, dissolved by heating.

Mix the above solutions with distilled water, before using, in the proportions—

(a) 15 c.c. ; (b) 10 c.c. ; distilled water, 30 c.c.

and filter.

5. Wash the preparation in the ordinary manner with water. Examine in water, and if satisfactory mount in xylol balsam. The advantage of examining the specimen in water is that in it the flagella appear more distinct than in balsam, and, if too faintly stained, the specimen can again be placed in the orcein solution, and the process repeated.

181. *Zettnow's method* (*Zeitschr. f. Hyg.*, Bd. xxx. S. 95) gives very satisfactory results.

Prepare the following solutions:—

1. *Mordant*—

(a) Tannin	5 grms.
Aq. dest.	100 c.c.

Dissolve in a flask kept in a water-bath at a temperature of from 35° to 40° C.

(b) Tartar emetic. 1 gm.

Sufficient distilled water to dissolve this when heated in a test-tube.

Add (b) drop by drop to (a) until the precipitate formed is no longer dissolved by shaking, and filter. The solution obtained should be opalescent, but should allow of the passage of transmitted light. It should become quite clear on being heated slightly. Should the cold solution throw down any precipitate, add a drop or two of solution (a) and warm. Add a few crystals of thymol as a preservative.

2. Ethylamin Solution—

(c) Silver sulphate	2 grms. ¹
Aq. dest.	200 c.c.
(d) Solution (c).	1 part
Aq. dest.	1 „

To solution (d) add a 30 per cent. watery solution of ethylamin, until the brown precipitate formed is dissolved and the fluid is perfectly clear, then add solution (c) carefully, drop by drop, until a precipitate of oxide of silver is formed. This first dissolves easily on shaking, but then with greater difficulty. The addition of solution (c) should be stopped before the precipitate becomes permanent. If too much silver sulphate is used, the solution becomes yellow, and a deposit of small dark brown crystals occurs when heat is applied; correct by adding $\frac{1}{2}$ to 1 drop of ethylamin and start afresh with the silver sulphate. The excess of ethylamin, on the other hand, should be as slight as possible, otherwise the sensitiveness of the reaction is interfered with. Solution 2. is stable and very active.

Films are best prepared from a forty-eight hour culture or in the case of the cholera vibrio from a sixty-hour culture. An excellent emulsion may be obtained by adding a loopful of culture to a little salt solution or distilled water in a watch-glass. Allow to stand for five or ten minutes, and add one or two loopfuls of osmic acid 2 per cent. solution. Prepare films in the ordinary way. These films may be washed in 5 per cent. acetic acid after they have been fixed. Zettnow, however, recommends the following:—

Make a broth culture of the organisms to be examined. In from

¹ Pure silver sulphate may be prepared from silver nitrate as follows:—Dissolve 5 grms. of silver nitrate in 30 c.c. aq. dest. Add to the cold and clear solution 5 grms. of magnesium sulphate. Let the mixture, from which a heavy deposit of silver sulphate separates, stand for half an hour; pour off the supernatant fluid, and wash in three or four changes of distilled water, allowing the flask to stand about one minute after each washing. Place the silver sulphate in a clean flask with 500 c.c. of distilled water, and in about an hour we have a saturated solution.

ten to twenty hours examine the culture under the microscope, and as soon as motile organisms can be seen pour off the culture into a 4 per cent. formalin solution contained in a conical sedimenting glass, taking care to keep back any sediment that may be present. At the end of twenty-four hours the larger organisms and coarser masses have settled and may be examined. The fluid poured off from the surface should then be sedimented in another glass for forty-eight hours, in some cases even longer. Pour off the supernatant fluid and wash the sedimented organisms with 1 per cent. formalin in distilled water, allow to settle, decant the supernatant fluid, and again wash the organisms with 1 per cent. formalin, again pour off the supernatant fluid and repeat the washing, but this time with pure sterile water, in order to remove all traces of formalin which even on the cleanest glass surface causes the fluid to run into drops instead of spreading out into a film. As the percentage of formalin is lowered, sedimentation goes on more quickly. After the final sedimentation, pour off the fluid, and from the fine sediment prepare a series of films on cover-glasses; allow them to dry and fix by moderate heat.¹

After washing the film preparation in water, float it, film side downwards, upon the mordant contained in a covered capsule, place this on a hot plate, and keep for from five to seven minutes at about 100° C. Allow the capsule to cool down until the mordant begins to become turbid, then remove the specimen and wash carefully in water.

Now filter on to the film 4 or 5 drops of ethylamin solution, and warm the cover slip until steam rises freely and the edges of the film become blackened. Then examine in water under the microscope to see that the flagella are properly stained. If they have come out sufficiently deeply, wash and mount permanently. If the flagella and bacteria are distinctly yellow, the preparation has not been heated enough. If any granular precipitate is seen on the film it has been heated too much. For bringing out very fine flagella, the action of the mordant may be intensified by rendering the solution neutral or faintly alkaline to litmus by the addition of dilute caustic soda *just before the mordant is used.*

182. Sections to be examined for *tubercle bacilli* should be hardened in formalin and alcohol. Sputum or other fluids should be examined as cover-glass preparations. Take a small quantity of any

¹ The sediment may be stored in 1 per cent. formalin.

of these fluids with a needle or platinum loop and smear it on a cover-glass, press another against it, and wipe away any superfluous fluid that may appear at the edges with a bit of blotting paper. Separate the cover-glasses, when each will be found to be covered on one side with a very thin film. Allow this to dry, and then, if the material contains any albumin, holding one of the cover-glasses in a pair of forceps, pass it several times through the flame of a spirit lamp, by which process the albumin is coagulated. In the case of sputum a small purulent or caseous portion, if such be present, should always be selected, and removed with a pair of forceps, and, as it is somewhat difficult in certain cases to spread out the sputum on the cover-glass, it is well to adopt Kühne's method of diluting it with a concentrated solution of borax. The borax solution and sputum are taken in equal parts and thoroughly shaken in a suitable glass vessel, or worked up in a mortar, after which it is an easy matter to spread the mixture in a thin layer on the cover-glass in the ordinary manner. Nummular sputa from cavities may also be broken down by the addition of a watery solution of carbonate of ammonia; this substance is partially volatilised as soon as the cover-glass is heated, and what remains is broken up by the acid in the after-treatment of the specimen.

Van Ketel's method (*a*) may be used when sputum is watery, copious, or purulent, or Biedert's method (*b*) when sputum is mucous, atypical, or scanty.

Strangeways describes these methods—(*a*) Add 5 c.c. of liquid carbolic acid to 100 c.c. of sputum in a flask, shake thoroughly, centrifugalise, or allow to stand in a burette for twenty-four hours. Prepare films of the sediment dry, "flame," and then soak in chloroform for a couple of minutes, wash in water, "blot" and again "flame." Stain by the Ziehl-Neelsen method (§ 183). (*b*) In a small beaker add 30 c.c. of water to 15 c.c. of sputum; constantly stirring, add a little 10 per cent. caustic soda (4 to 8 drops). Boil slowly, adding 60 to 90 c.c. of water until the mixture is thin enough. Centrifugalise or allow to stand in a burette or conical glass for twenty-four hours or longer. Mix with a little Mayer's albumin solution (§ 98), make films, and stain as above, taking care to leave the film somewhat longer than usual in the fuchsin solution.

183. *The Ziehl-Neelsen method of staining the tubercle bacillus.*—This is a modification of the Weigert-Ehrlich method, which is now

seldom used, and from which it differs in being a permanent stain. The sections or cover-glass preparations or films are stained in Neelsen's solution, made as follows:—Fuchsin, 1 part, dissolved in 10 parts of alcohol, to which solution 100 parts of a 5 per cent. watery solution of carbolic acid are added; this is heated until steam rises pretty freely. The cover-glass preparations are stained in three or four minutes, or even less; sections are usually sufficiently deeply stained in seven or eight minutes. In the cold, they may be left for twelve or even twenty-four hours. The superfluous fluid is drained off, and the preparations are placed for a second or two in alcohol (90 per cent.), then in a 25 per cent. solution of sulphuric acid, when the pink tinge should immediately be replaced by a yellowish-brown. The preparations are then washed in alcohol, and if they are sufficiently decolorised they are transferred to a solution of lithium carbonate. They may afterwards be stained with a watery solution of methylene-blue, or with methyl-green (§ 130), cleared up with clove or anilin oil, turpentine, and xylol, and mounted in Canada balsam (§ 199). Exceedingly good results are obtained by this method, which is preferable, in many respects, to the anilin oil method. *Leprosy bacilli* in tissues may be stained by the above method, but they are decolorised too rapidly by the comparatively strong acid. A 5 per cent. solution of sulphuric acid followed by rinsing in water—no alcohol should be used at this stage—gives the best results. Even after the counter-staining with methylene-blue, the process of dehydration by alcohol should be carried out as rapidly as possible.

184. In place of sulphuric acid, nitric or hydrochloric acid may be used, and for clinical work, in order to shorten the process, the methylene-blue may be mixed with the acid, the decolorising and contrast staining being carried on in one process; this is strongly recommended by Fränkel, Gabbet, and Lieberman. It is certainly very convenient for clinical work, and gives excellent results. After staining in carbolic acid fuchsin (§§ 120 and 183) and washing thoroughly with distilled water, keep the covers for one minute in the following solution:—

Methylene-blue	1·5	gram.
Absolute alcohol	30	c.c.
Sulphuric acid	20	„
Distilled water	50	„

Wash in water or in weak alcohol, and examine fresh, or mount in balsam (§ 199).

185. To demonstrate tubercle bacilli in tuberculous milk, the best plan is to treat the milk with eau de Javelle and ether; centrifugalise and take the sediment for examination, when almost the whole of the bacilli that were originally in the milk will be found along with other bacteria and solid particles in this sediment. This method, devised by Bevis and Moore, is carried out as follows:—

To 50 c.c. of the milk to be examined add 5 c.c. of methylated ether in a glass cylinder of 150 c.c. capacity; mix thoroughly and then add 20 c.c. of eau de Javelle prepared as follows: triturate 20 parts of good fresh bleaching powder in a mortar in 100 parts of water; dissolve 20 parts of dry, not crystallised, potassium carbonate in 100 parts of water; mix thoroughly, allow to stand for an hour, and filter the supernatant fluid under pressure. The cylinder containing the milk mixture is allowed to stand in water at 100° F. for from fifteen to thirty minutes; it is then cooled and 30 c.c. of a mixture of 1 part rectified spirit and 2 parts methylated ether added; the whole is again thoroughly mixed, and the brown liquid is centrifugalised. The deposit from a series of tubes may now be washed into a clean tube; to this deposit 6 or 7 drops of a 10 per cent. solution of sodium carbonate are added, and the tube is filled up with distilled water to which 10 to 15 c.c. of ether, to remove the last traces of fat, have been added; the mixture is again well shaken, again centrifugalised, and a microscopic examination made after staining by the Ziehl-Neelsen method (§ 183). The microscopic films should never be too thick, or the few isolated tubercle bacilli may be obscured by the large number of other organisms. The process is so easily carried out that a large number of samples and thus a large quantity of milk may be passed under examination very quickly. The authors of this method recommend that Winter Blyth's water sediment tubes should be used for rotation.¹

Where it is not possible to obtain the use of the above apparatus, the milk should be allowed to stand for from twelve to twenty-four hours in a glass "separator," such as is used by chemists, or in a conical or funnel-shaped vessel, surrounded by ice. The sediment with the contained bacilli is drawn off from the separator by the tap placed at

¹ *Journ. Path. and Bact.*, Edinburgh, 1901, vol. vii. p. 293.

its lower part, or the cream and the upper layers of the milk may be carefully removed by means of a syphon, then with a pipette a few drops of the milk from the bottom of the funnel are taken, dried on a cover-glass, and examined in the ordinary way. In place of the separator or other funnel-shaped vessel, I have used, at Mr. Coghill's suggestion, a long wide burette (which can usually be obtained), in which to allow the milk to stand. In drawing off the sediment from the separator or burette, the first few drops are rejected, the fluid from immediately above the stop-cock, which contains most of the bacilli, being taken.

186. *Neisser's stain for the diphtheria bacillus.*—Incubate the organism for eighteen hours on blood serum, stain films, fixed by heat, for two minutes in the following solution:—

Powdered methylene-blue (Grübler)	1 part.
Alcohol, 96 per cent.	20 parts.
Distilled water	950 „
Glacial acetic acid	50 „

Filter.

Wash the film well in water, and stain for two minutes in 1:500 solution of vesuvium made with boiling water, wash, dry, and mount in Canada balsam (§ 199). The diphtheria bacilli appear as pale brown rods in which are bluish-black, oval, polar, rarely central granules.

187. *Nicoll's stain for the diphtheria bacillus.*—

Saturated alcoholic solution of gentian-violet	10 parts.
1 per cent. watery solution of carbolic acid	100 „

The fixed cover-glass preparation remains in the stain for about five seconds, and is then passed directly into Lugol's iodine fluid (§ 42), 1:2:200, where it remains for about five seconds; after this it is decolorised and dehydrated by being passed rapidly through a mixture of one volume of acetone with four volumes of absolute alcohol; this removes all unfixed stain, almost instantly. Clear in xylol (§ 193), allow to dry, and mount in balsam (§ 199).

188. *To stain the glanders bacillus in cover-glass preparations.*—Cover-glass preparations of farcy pus or material from glanders

nodules containing glanders bacilli may be stained with any of the ordinary basic anilin dyes—methylene-blue (§ 115), gentian-violet (§ 118), fuchsin (§ 120), thionin-blue (§ 122). The nuclear detritus in these preparations is then decolorised for from five to ten seconds by a 4 per cent. solution of acetic acid. The bacilli still retain the stain; examine at once or mount in balsam (§ 199).

To stain the glanders bacillus in sections.—

Noniewicz's method.—Place sections for from one to five minutes in Loeffler's methylene-blue (§ 115), wash in distilled water, and then decolorise for from one to five seconds, according to the thickness of the section, in a mixture of 75 parts of a 0·5 per cent. solution of acetic acid and 25 parts of a 0·5 per cent. watery solution of tropæolin; wash again in distilled water, and, after spreading the section on a slide, dry it, first with blotting paper, and then in the air or over a spirit flame. Clear by dropping xylol upon the section (oil of cloves, origanum, and anilin oils must be avoided), and mount in Canada balsam (§ 199). The bacilli are stained dark blue or nearly black, and the tissue light blue.

M'Fadyean's method.—To obtain good differential staining in bacilli contained in sections Sir J. M'Fadyean uses the following modification of the tannic acid mordanting method, which appears to be greatly superior to any other method yet recommended. Harden in alcohol (§ 58) and embed in paraffin (§ 94). Stain very thin sections for half an hour in either Kühne's carbolised solution of methylene-blue (§ 172), Loeffler's alkaline solution (§ 115), or in a 1 per cent. solution of this blue in 10 per cent. alcohol; rinse in water and then transfer to a 4 per cent. solution of acetic acid in water for a few seconds, and again rinse in water; "the acid solution almost entirely decolorises any normal tissue surrounding the lesion, and the latter is reduced to a pale blue"; then immerse the section for fifteen minutes in a saturated aqueous solution of tannic acid, wash thoroughly and stain for from fifteen to thirty seconds in a 1 per cent. aqueous solution of acid fuchsin, wash in water, dehydrate, clear in cedar-wood oil (§ 193), and mount in xylol balsam (§ 199). "In sections thus treated the nuclei and nuclear detritus in the lesion have almost entirely lost the blue stain and the tissues are for the most part of a faint red, while the bacilli are of a light blue colour."

OTHER REAGENTS USED IN THE PREPARATION AND MOUNTING OF SECTIONS

189. *Acetic acid.*—One part of glacial acetic acid to four parts of water is extremely useful for dissolving albuminoid substances in fresh tissues, and for bringing the nuclei of certain cells, such as pus cells or white blood corpuscles, into special prominence. It is also used for rendering sections of tissues, such as lymphatic glands or the spleen, more transparent. It seems to act by dissolving or causing swelling of the ground substances, thus rendering them homogeneous, and throwing up certain structures, nuclei, elastic fibres, myelin, and micro-organisms into greater prominence. It may be used to neutralise logwood when the stain is too deep (§ 113), and a weak solution (1 drop to the ounce) (§ 105) to fix carmine in the tissues by precipitation (where strong carmine is used as a rapid staining reagent) before the sections are washed and mounted.

Beale's mixture of glycerin, 1 oz., and glacial acetic acid, 5 drops, may also be used for clearing up tissues in the manner above recommended.

190. *Caustic potash or soda,* 40 per cent. solution, is extremely useful for clearing up sections of fresh tissues, or any tissues which are to be mounted in glycerin or Farrant's solution, both of which fluids again, having a higher refractive index than water, increase somewhat the transparency of tissues. It alters the ground substance and the cells, and throws elastic fibres and bacteria into relief. Reference has already been made to its use in separating muscular fibres (§ 44).

191. *Ether and chloroform.*—These fluids are especially used for dissolving out fat from tissues. When such tissues are fresh it is necessary to drive out the water, by which the fat is protected from the action of the ether or chloroform, by means of absolute alcohol.

Place the section in a watch-glass containing absolute alcohol until all the water is removed (which will be the case as soon as the milkiness disappears), when the section should be transferred to a vessel containing ether or chloroform. Allow it to remain in one of these fluids for a few minutes, and transfer first to alcohol, then to a weak solution of acetic acid; stain and mount.

192. *Bicarbonate of soda*, 5 per cent. solution, is used principally for the purpose of neutralising the acid-hardening fluids (picric acid or chromic acid) before staining with such reagents as logwood. This is done after the sections are made. This solution also removes much of the yellow picric acid stain. Staining may then be proceeded with in the ordinary manner.

CLEARING FLUIDS

193. As the methods of mounting and staining have become more complicated, numerous clearing agents have been introduced for the purpose of bringing certain of the tissue elements into greater prominence.

Most of the clearing fluids have a high refractive index, and saturating the tissues, so "clear" them that the greater part of the tissue picture is lost, only the stained portions being brought into prominence. Glycerin (§ 194) and acetate of potash are both of them useful in this way; Farrants's solution (§ 195), which contains a considerable proportion of glycerin, is often used as a mounting fluid. These clearing substances are used where it is not desired to have the tissues too fully cleared.

Other clearing reagents, ethereal oils and certain coal-tar products, are selected according to the kind of stain which has been employed and the substance used in embedding the sections. Most of these clearing reagents either dissolve celloidin or will not clear it from 95 per cent. alcohol, and in many of them anilin colours are more or less readily soluble. Almost any of the ordinary clearing reagents may be used to clear sections stained in hæmatoxylin or carmine.

Clove oil and turpentine were the first of the ethereal, etc., oils employed to render stained tissues more transparent before mounting them in Canada balsam or in dammar varnish. Clove oil, one of the most active of the volatile oils, is very frequently used, and is very agreeable to work with; it is, however, a powerful solvent of anilin colours, so that where the tissues are stained with these dyes, turpentine, anilin oil, and xylol, carbolic acid, creosote, bergamot oil, cedar-wood oil, origanum oil, lavender oil, etc., may be used in its place. Before oil of cloves or any other of these clearing reagents can be applied to the section, all water must be abstracted by means of absolute alcohol. The procedure is as follows:—After

staining the section, wash well in water to remove all the staining fluid not actually taken up by the tissues; pour about a drachm of absolute alcohol into a watch-glass, and into a second, a similar quantity of the clearing reagent; remove the section from the water with a needle, and absorb from it as much of the moisture as possible by means of a piece of blotting paper or a soft cloth, allowing the free end of the section just to touch one of these absorbent materials; place the section in absolute alcohol, allowing it to remain for two or three minutes without attempting to spread it out; then transfer with a dry needle to the ethereal oil (clove, bergamot, etc.), when the alcohol, rapidly diffusing, carries the edges of the section with it, and in this way the section is spread out on the surface of the fluid. It must not be left for an instant after it is clarified—(this should never take longer than half a minute if the section has been properly dehydrated)—as certain of these oils render the tissue extremely brittle and friable. To transfer the section to the slide, pass the blade of the copper lifter, after carefully smearing it with the clarifying medium, under the section as it is spread out on the surface of the oil, fix one margin of the section with the point of a needle and lift it from the watch-glass; have the blade as nearly horizontal as possible, so that the section still floats in oil on the blade; bring the blade down parallel on to the slide, *which must be perfectly dry*, and, fixing the edge of the section with the point of the needle, gently *withdraw* the copper lifter, leaving the section on the slide. Tilt the slide to allow any superfluous oil to drain off, dry carefully with a soft cloth, put on a drop of Canada balsam or dammar varnish, lower a cover-glass on the section, and press it down with the handle of the needle—any air-bubbles which may have become entangled in the tissues being by this means driven out. In a day or two the cover-glass becomes fixed, and the preparation will bear any amount of knocking about. For the carbolic acid and xylol method, see § 100. Sections fixed on cover-glasses or slides are, of course, much more easily handled. When on a cover-glass, after being dehydrated and cleared, the section is simply “picked up” by a drop of the mounting medium placed on the centre of a slide. This slide inverted and lowered on to the section as it lies on the cover-glass takes both up very readily and accurately.

Weigert's mixture of anilin and xylol (§ 140) may be used especially for clearing thick carmine- or hæmatoxylin-stained sections of the

central nervous system. Where anilin stains are used the best clearing reagent is xylol, which, however, clears only when absolute alcohol has been used to dehydrate. It can be used for celloidin or other sections kept in 95 per cent. alcohol in the following fashion. Blot the section on the slide with smooth, soft filter paper, and then pour on a few drops of xylol; repeat the process two or three times, and then mount; never use oil of bergamot to clear eosin-stained sections or oil of cloves for methylene-blue stained specimens. Indeed, with most anilin stains use cedar-wood oil, anilin, or xylol. For celloidin or paraffin sections stained with hæmatoxylin or carmine, oleum origanum cretici (never use the ordinary origanum oil) or oil of bergamot may be employed.

A very good clearing fluid which may take the place of these is one recommended by Dunham for celloidin or paraffin sections stained by hæmatoxylin or carmine. It consists of

Oil of cloves	1 part.
Oil of thyme	4 parts.

Filter if cloudy.

This has the great advantage that though it clears up celloidin sections from 95 per cent. alcohol it does not dissolve the celloidin.

MOUNTING MEDIA

194. *Glycerin*, or some fluid in the composition of which glycerin is an important constituent, is the most useful fluid for the preservation of thin sections which are to be transferred at once from water to the slide. Where pure glycerin alone is used, as for extremely delicate tissues (thin sections of lung or peritoneum), the section is placed on the slide (§ 43), superfluous moisture is drained away or removed with a soft cloth, and a small drop of the fluid is run on to the section from a glass rod; the size of this drop can only be determined experimentally, but it is always better to err on the side of too large a drop, as air-bubbles are not then such frequent intruders under the cover-glass. Lower the cover-glass on to the section (§ 38) and press down gently with the handle of the needle to expel air-bubbles, which, with glycerin, only too frequently get in, and are then with very great difficulty driven out. All superfluous fluid at the margin of the cover-glass must be removed with the aid of a small glass pipette, and a

brush slightly moistened with water; the slide should be carefully dried with a soft cloth, and cemented in the course of an hour or two. The advantages of glycerin as a mounting fluid are its simplicity and its clarifying property, in the case of sections unstained, or stained with the metallic staining reagents, and more particularly in the case of those tissues which are to be examined with high powers. Its disadvantages are, that it is extremely hygroscopic and does not dry, and so does not fix the cover-glass, that it sometimes clears up sections too much, and that it causes fresh white fibrous tissue to swell and look almost gelatinous. In place of glycerin, Farrants's gum and glycerin fluid is now usually employed.

195. *Farrants's mounting fluid*.—Take of

Water,

Glycerin,

Arsenious acid, saturated solution (satu-

rated by boiling) equal parts.

Mix well in a covered jar, and add about half the bulk of picked gum-arabic; allow this to stand for three weeks, stirring daily, or until the whole of the gum is dissolved. Then filter through coarse filter paper, or allow the filtrate to stand for a further period of a couple of weeks, when the air-bubbles will have come to the surface, and any dirt will have settled to the bottom. Decant, as required, into a 1-oz. stoppered phial, to the stopper of which a glass rod is fused. Use in the same way as glycerin. If too much gum be used, the tissues are apt to become slightly granular, whilst, if glycerin is in excess, the tissues become transparent, and the solution does not dry properly at the edge of the cover-glass, which remains unfixed.

This mounting medium, though it has now almost gone out of fashion, is one of the most useful of all the media for preserving all but "completely" clarified sections for microscopic examination. It combines most of the advantages of glycerin with few of its disadvantages. It does not cause such marked swelling of fresh tissues, nor does it render sections quite so transparent as does the glycerin, though it clears them up very appreciably, especially after they have been mounted for a few days. It also acts as a preservative medium, on account of the presence of the arsenious acid; and the glycerin, by its affinity for water, keeps the section moist, until the fluid at the edge of the cover-

glass dries. By this drying the cover-glass is fixed slightly by the gum, and after the specimen has been mounted for two or three days, the slide may be cleaned, and the cover-glass cemented with Hollis's glue or indiarubber solution. The only real disadvantage of this fluid is that sections kept in it for a number of years may become somewhat cloudy and slightly granular, though some of my picro-carmin stained specimens preserved in this medium are even more brilliant and demonstrative than they were when they were mounted twenty-five years ago.

196. *Camphor mounting fluid*, recommended by Hamilton, is sometimes used in place of Farrants's solution, in which to mount sections stained or injected with fluid that might be affected by arsenious acid. For instance, sections taken from an organ injected with Prussian blue must be mounted in a fluid which contains no arsenious acid, that substance causing decolorisation of the iron blue.

This fluid consists simply of Farrants's medium, in which the arsenious acid solution is replaced by camphor water. Take of

Camphor water	2 parts.
Glycerin	1 part.
Pure picked gum-arabic	1½ „

Prepare as for Farrants's solution, and keep a piece of camphor floating in the fluid. Employ as glycerin or Farrants's solution.

197. *Glycerin jelly*—

Pure gelatin	30 parts.
Distilled water	70 „
Glycerin	100 „
Alcoholic solution of camphor	5 „

Allow the gelatin to stand in the distilled water for from twelve to twenty-four hours, until perfectly softened, boil and strain through a warm filter or a felt jelly bag, add the glycerin and the camphor, mix thoroughly, and warm as required. Be very careful to avoid air-bubbles, and to keep the slide warm until the cover-glass is in position. Keep the medium in small bottles, and when it is to be used, immerse in water warm enough to keep it fluid.

198. Richard Muir has devised the following method for mounting and preserving delicate tissues, parasites, ova, embryos, renal casts, many kinds of crystals, and, indeed, any kind of microscopic object which must be preserved in a watery medium.

The following is the medium used :—

Thymol water (saturated in the cold)	. . .	100 c.c.
Glycerin (pure)	5 „
Acetate of potash	0.5 grms.
Gelatin (Coignet's)	10 „

Soften the gelatin in a water bath, add the glycerin and acetate of potash, and render the mixture acid with acetic acid. Clear with white of egg and filter. The material to be mounted is collected in a watch-glass and mixed with 5 to 10 per cent. solution of formol (Schering). At the end of about an hour the formol is drained off and a little water (distilled) is added. This is then run off, and if the object is to be stained, hæmatein or safranin (these stains give the best results) is added. On the centre of a clean slide put 2 or 3 drops of the softened gelatin medium with a platinum loop, add a loopful of strong formol to the liquid gelatin medium and mix on the slide : transfer the material from the watch-glass to the medium on the slide. Embed completely in the gelatin and cover with a clean cover-glass. When the gelatin has set, which it does very rapidly, the specimen may be cleaned and ringed with Canada balsam.

CANADA BALSAM AND DAMMAR VARNISH

199. These mounting fluids may both be used for deeply stained sections, especially where it is necessary to bring into strong relief the stained parts of the tissue. They can be used only where the tissues have been previously dehydrated with alcohol, and cleared up with some substance (clove oil or turpentine) (§ 193) with which they will amalgamate. Each fluid has its special advantages and each its disadvantages, one of the latter being that Canada balsam has a somewhat yellow tint, and hence is said not to be fitted as a mounting medium for sections that are to be photographed, but sections mounted in it keep perfectly well for years. If properly prepared, and not too thick, this is merely a theoretical drawback, as I have seen most beautiful photographs of sections mounted in Canada balsam. This

medium is now most frequently used when dissolved in xylol, which does not affect anilin colours. Having a high refractive index, it keeps all tissues, except those stained, very transparent. To prepare Canada balsam mounting fluid, heat the ordinary Canada balsam gently for about twenty-four hours in a covered vessel; allow it to cool to a yellow vitreous looking mass;

Take of this	100 parts.
Xylol	90 „

Dissolve, and filter through fine cotton wool. The fluid must be kept in a stoppered bottle which has previously been carefully dried, and rinsed out first with absolute alcohol, and then with xylol. It must be kept in a dry place.

It is well to bear in mind that tissues stained with osmic acid should always be mounted in balsam, in which chloroform takes the place of xylol.

200. Sections mounted in dammar varnish, as a rule, become somewhat cloudy and granular after they have been kept for a year or two; but when fresh they are beautifully transparent, and the medium itself is perfectly free from colour, so that it is admirably adapted for photographic work.

Dammar varnish is prepared as follows:—Take of

Gum dammar	2 parts.
Gum mastic	1 part.
Turpentine	4 parts.
Chloroform	2 „

(These proportions give very good results, but may be varied somewhat as a thinner or a thicker fluid is preferred.)

Mix in an earthenware jar or wide-mouthed bottle, stirring and agitating until the gums are dissolved, then filter through coarse filter paper into small stoppered phials, to the stoppers of which glass rods have been fused.

For mounting Golgi preparations, dammar varnish dissolved in xylol or chloroform is usually recommended.

Colophonium dissolved in benzine, although recommended merely for mounting Nissl preparations of nerve cells, might often be used with advantage for other sections.

CEMENTING OF COVER-GLASSES

201. For this purpose various solutions have been suggested, but the same great difficulty almost invariably presents itself, that whatever substance is used the glycerin, sooner or later, leaks out. With Farrants's solution there is not the same difficulty, it being quite sufficient, after careful cleaning of the slide, and allowing the gum in the Farrants's solution to partially fix the cover-glass, to run a ring of gold size, French glue, Hollis's marine glue, or indiarubber solution around the margin of the cover-glass. It may then be left for twenty-four hours, after which a ring of zinc white cement may be laid over the ring already painted on, and this may be repeated in the course of a day or two, when the first layer has become properly set.

202. Zinc white cement is composed of—

Benzole	8 parts.
Gum dammar	8 „
Oxide of zinc	1 part.

Mix the gum dammar, and the benzole, filter through cotton wadding, after which add the oxide of zinc, mix in a mortar, and again filter through the wadding.

This cement forms a very workable material, and when set is as hard and firm as enamel. After a time, however, it usually becomes brittle and cracks, and it is far the best plan to use it in combination with one or other of the cements already mentioned.

Slides treated in this manner will, if properly cemented in the first instance, keep perfectly free from leakage for years.

203. In applying these various rings, it is well to use a "turn-table." This is a heavy brass disc about $3\frac{1}{2}$ inches in diameter, which should work smoothly on a conical-pointed pivot fixed to a solid piece of wood. On the disc are usually marked or engraved a series of concentric rings, each of which should correspond in size to one of the ordinary cover-glass sizes. A couple of brass clips are affixed, which serve to keep the slide in position when the cover-glass is "centred." Self-centring turn-tables are now also much used. With a goat's-hair brush or short stiff camel's-hair pencil lay on first a ring of the size or other cement, and when this is dry, paint on a ring of the

zinc white. In working with these cements, always keep the brushes clean. This is most conveniently and thoroughly done by means of warm water for the size, glue, or gelatin, and turpentine or benzole for the zinc white. When the zinc white becomes too thick to run readily, it may be diluted with benzole.

204. Label the slide with the name of the tissue, the disease, date of post-mortem examination, method of staining and mounting employed, and the date of mounting. It is now ready for future examination. Slides so prepared should be kept in the flat trays mentioned below, carefully protected from both light and dust.

205. In addition to apparatus mentioned (§ 34), the following will be required :—

- a. A razor and a couple of scalpels, similar to those already procured. (§ 1.)
- b. Three or four strong needles firmly set in hardwood handles. These should be quite smooth, free from rust, the point perfect, and not hooked or twisted. They should, from time to time, be cleaned with emery paper, and then with chamois leather. Glass rods, drawn out to points, and blunted, curved, or straight, or platinum iridium needles, may, with advantage, be used instead of these needles.
- c. A couple of pairs of scissors ; one pair straight and probe-pointed, the other pair sharp-pointed and curved on the flat. Those used by the ophthalmic surgeon answer the purpose admirably.
- d. A copper lifter, with a stem about $3\frac{3}{4}$ inches long, and two blades—one about 1 inch \times $\frac{3}{4}$ inch, and the other $\frac{5}{8}$ inch \times $\frac{3}{8}$ inch. The stem should be flat and the blades, continuous with it, very thin, so that they may be bent to form any angle. The edges must be perfectly rounded and smooth. Nickel and platinum lifters, now made of very good quality, may be used instead of the copper lifters.
- e. Six or a dozen deep watch-glasses, or “Syracuse” glasses with flat glass covers.
- f. Two or three test-glasses and half a dozen test-tubes.
- g. Two or three white earthenware or enamelled iron pint basins, two or three glass or enamelled iron “tumblers,” and about a dozen rounded shallow glass trays or capsules.

- h. Two or three small glass tube pipettes, for removing fluids of various kinds from the edges of the cover-glasses after sections have been mounted.
 - i. Several goat's-hair pencils for cementing slides, and a similar number of camel's-hair pencils for the manipulation of sections, in the process known as pencilling.
 - j. Glass slides with ground edges, 3 inches \times 1 inch.
 " " " 3 inches \times 1½ inch.
 Extra thin circular cover-glasses, $\frac{7}{8}$ inch in diameter.
 " " " 1¼ inch diameter.
 Square cover-glasses for use when Canada balsam is the mounting medium.
 - k. Labels for slides.
 - l. A small box for carrying six or a dozen slides, and a cabinet to hold about ten dozen slides, should be obtained, in order that the specimens may be kept clean and well arranged.
 - m. A soft linen cloth. An *old* pocket handkerchief is, perhaps, the best cloth one can use.
 - n. Drawing materials. A couple of black lead pencils—HB and HHHH.
 Half a dozen lithographic pens.
 Box of coloured crayons or chalks.
 A small box of moist water colours (which may be used as inks with the lithographic pens), with brushes.
 Some ordinary mounts to be cut into drawing cards.
 - o. Two or three packets of white filter papers.
 - p. A microtome (§§ 88, 89, 92, and 96).
 - q. A spirit lamp or Bunsen burner.
- For embedding in paraffin or celloidin, the following additional apparatus will be required :—
- r. A small copper water oven, with thermometer and gas regulator, in which a temperature of from 52° to 60° C., as required, may be maintained.
 - s. A packet of silk "kitchen" paper.
 - t. Two or three "whole plate" photographic "developing" dishes.
 - u. A few blocks of wood, 1 inch or more square, cut across the grain.
 - v. "Angle" pieces of metal for use as embedding boxes.

LISTS OF REAGENTS AND WORKS FOR REFERENCE

206. The following reagents, which should be in 1-oz. glass-stoppered bottles, will also be required. Those marked *R* should be kept in retort-shaped "drop" bottles, or in narrow-mouthed stoppered bottles; to these stoppers a glass rod is fused. The end of this rod must be well rounded, *not* pointed. Those marked *W* should be in wide-mouthed glass-stoppered bottles.

REAGENTS IN GENERAL USE

- R.* Ranvier's picro-carmin staining fluid (§ 102, p. 80), or
Van Gieson's stain (§ 103, p. 82), or
Picro-erythrosin (§ 104, p. 83).
Hæmatein or hæmatoxylin staining fluid (§ 108 *et seq.*, p. 85 *et seq.*).
- R.* Carmine staining fluid (§ 105, p. 84).
Alum carmine (§ 106, p. 85).
Methyl-violet (§ 117, p. 90).
Loeffler's methylene-blue or toluidin-blue (§ 115, p. 89).
Gentian-violet (§ 118, p. 91).
Carbol-fuchsin (§ 120, p. 92).
Thionin-blue (§ 122, p. 93).
Jenner's eosin methylene-blue stain (§ 151, p. 114).
Leishman's stain (§ 153, p. 115).
- R.* Lugol's iodine staining fluid (§ 42, p. 46, and § 133, p. 98).
Eosin, $\frac{1}{16}$ per cent. solution (§ 132, p. 97).
- W.* Osmic acid, 1 per cent. solution (in bottle covered with brown paper) (§ 44, p. 48, and § 135, p. 99).
Sudan III. or Scharlach R (§§ 135*a* and *b*, p. 100).
Acetic acid, 1 to 20 per cent. (§44, p. 49, and § 189, p. 144).
- R.* Glacial acetic acid (§ 189, p. 144).
- R.* Caustic potash, 40 per cent. (§ 44, p. 48, and § 190, p. 144).
Ether (§ 191, p. 144).
Chloroform (§ 191, p. 144).
Neutral saline solution, $\frac{3}{4}$ per cent. solution of common salt (§ 36, p. 43).
Bicarbonate of soda, 5 per cent. solution (§ 192, p. 145).
Absolute alcohol (§ 58, p. 59, and § 193, p. 145).
- * Anilin oil (§ 118, p. 91).
- R.* Oil of cloves, xylol, creosote, and turpentine (§ 193, p. 145).
Clearing solution (§ 103, p. 83).
- R.* White of egg and glycerin (§ 98, p. 78).
Solid paraffin—hard and soft (§ 94, p. 76).
- W.* Celloidin (§ 91, p. 74; see also § 93, p. 75).
Large bottles containing—
Methylated spirit.
Distilled water.

MOUNTING FLUIDS

- R.* Farrants's solution (§ 195, p. 148).
R. Glycerin (§ 194, p. 147).
R. Iodine mounting fluid (§ 133, p. 98).
R. Canada balsam (§ 199, p. 150), or dammar mounting fluid, or colophonium (§ 200, p. 151).
W. Glycerin jelly (§ 197, p. 149).
R. Camphor mounting fluid (§ 196, p. 149).

CEMENTS AND SOLVENTS

- W.* French glue, gold size, or a solution of indiarubber (§ 201, p. 152).
W. Zinc white cement (§ 202, p. 152).
W. Benzole (§ 203, p. 152).

SPECIAL REAGENTS

- Liquor ammoniæ (for fungi, etc.).
 Lithium carmine (§ 107, p. 85).
 Lithium carbonate solution (§ 107, p. 85).
R. Carbonate of ammonia solution (§ 182, p. 138).
R. Borax solution (§ 182, p. 138).
 Saturated solution of oxalic acid (§ 117, p. 90).
R. Anilin blue-black (§ 128, p. 96).
 Bismarck-brown (§ 121, p. 92).
 Methyl-green (§ 130, p. 96).
 Safranin (§§ 124, 125; p. 94).
 Saturated solution of picric acid (§ 131, p. 97).
 Weigert's fibrin and elastic fibre stains (§§ 167, 168, 169, pp. 126-128).
 Pal's fluid (§§ 141, 142, p. 106).
 Ehrlich's stains (§§ 147, 148, pp. 111, 112).
 Giemsa's stain (§ 157, p. 119).
 Pappenheim's stain (§§ 161, 162, pp. 122, 123).
 Borrel's stain (§ 166, p. 125).
 Gram's iodine decolorising fluid (§ 173, p. 131).
 Ehrlich's iodine mixture (§ 133*a*, p. 99).
 Stains for flagella (§§ 178-181, pp. 133-138).
 Kühne's stains (§ 172, p. 131, and § 174, p. 132).
 Unna's alkaline methylene-blue solution (§ 116, p. 89).
 Benda's stain (§ 126, p. 95).
 Mordanting fluids (§ 178, p. 133 *et seq.*).
 Peroxide of hydrogen (B.P.) (§ 70, p. 65, and § 145, p. 109).

* Gold chloride, $\frac{1}{2}$ per cent. solution in distilled water (§ 136, p. 100).

* Silver nitrate, $\frac{1}{2}$ per cent. solution in distilled water (§ 137, p. 102), for tumours, etc.

* Perchloride of iron solution (§ 139, p. 103).

* The bottles in which these three reagents are kept should be carefully covered with brown paper, as should also the anilin oil bottle.

Nitric acid, 20 per cent. solution in distilled water (§ 44, p. 48).

Hydrochloric acid (§ 78, p. 68).

Sulphuric acid, 10 to 25 per. cent. solution in distilled water (§ 183, p. 139).

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CHAPTER III

INFLAMMATION, ORGANISATION, AND REPAIR

PRELIMINARY—CELLS FOUND IN THE BLOOD AND IN INFLAMED TISSUES

207. In making any examination of the blood or of tissues in which inflammation has occurred during life, several distinct cells are met with. It is unnecessary here to describe and illustrate all of them, but every student should be able to recognise, under the microscope, the more important of them.

Most of the cells of the blood can be readily obtained and fixed at once, and can therefore be easily examined fresh, and presumably little altered. The cells in the tissues obtained from the post-mortem room are, however, usually so far altered during the interval that elapses between the death of the patient and the post-mortem examination, that only the main features by which the cell may be differentiated remain.

Examine these cells at once, having found them under a low power, under a specially high power ($\times 800$). When their details have once been made out they may usually be recognised under the lower powers.

208. The *finely granular neutrophile or polymorpho-nuclear cell*, well seen in blood stained with Jenner's stain (§ 151), or by the Ehrlich Biondi method (§ 148), may also be found in the tissues, in the lymph spaces around blood vessels, and on free serous surfaces, especially during the earlier stages of an acute inflammatory process. It is usually a little larger than a red blood corpuscle, 9–12 μ in diameter, is more or less rounded, but has a somewhat irregular outline. The nucleus is often branching or divided into three or four irregular (polymorphous) lobes linked together by slender chromatin filaments. This nucleus is somewhat deeply stained as a whole, but on close

examination a well-marked chromatin network, in which the nodal points are deeply stained, may be seen, the inter-reticular substance being more delicately stained. The well-defined nuclear membrane takes on a fairly deep stain.

The cytoplasm or cell substance around the nucleus is colourless and transparent, unless the staining be very prolonged, but in its substance are fine granules that take on a feeble oxyphile stain, *i.e.* they are slightly stained by the acid dyes, eosin, etc. When examined

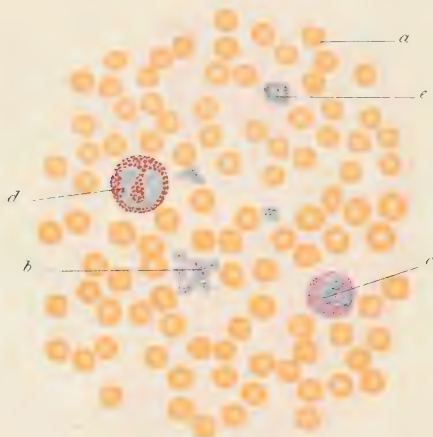


FIG. 4.—Blood cells in a film of normal blood stained with Ehrlich's triacid stain. ($\times 500$.) The leucocytes are somewhat flattened out, and appear larger than they really are owing to the method of preparation.

- a.* Red blood corpuscles.
- b.* Blood platelets.
- c.* Finely granular polymorpho-nuclear leucocyte with ϵ granules.
- d.* Coarsely granular eosinophile cell (α granules).
- e.* Small mononuclear cell or lymphocyte.

on the warm stage these cells change their shape, shoot out and draw in processes—they are in fact amœboid; they are also undoubtedly phagocytic, taking various foreign particles and micro-organisms into their substance. These cells are Metchnikoff's microphagocytes or microphages. They appear to play a very important part, as wandering cells, in acute inflammations, the facility with which they pass from

the blood vessels appearing to be associated with the marked lobulation of the nucleus which allows of the cell passing through a comparatively small crevice. These cells constitute 60-70 per cent. of the cells in normal blood. They are not found in the large serous cavities as a rule, but a few may be met with in the tissue lymph spaces. They constitute the majority of the cells of pus, but there appear to be undergoing degenerative changes. They are then less mobile than usual, and are often vacuolated.

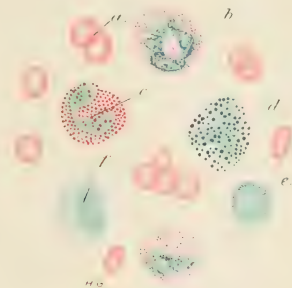


FIG. 5.—Blood cells in a film of normal blood, stained by Jenner's method. ($\times 600$.) Here the leucocytes are somewhat flattened out by the method of preparation of the film.

- a.* Hæmatocytes.—Red blood corpuscles.
- b.* Polymorpho-nuclear leucocyte with lobulated nucleus and ϵ granules in protoplasm.
- c.* Coarsely granular eosinophile leucocyte with bilobed nucleus and α granules in protoplasm.
- d.* Basophile cell with γ and δ granules.
- e.* Lymphocyte with large nucleus and a thin zone of granular or crenated protoplasm.
- f.* Mononucleated hyaline cell with kidney-shaped nucleus and hyaline protoplasm.

According to Beattie and others these cells quickly make their appearance in the peritoneal cavity under the stimulus of certain organisms such as the *Bacillus coli communis* introduced into that cavity. Within three hours they are numerous and actively phagocytic, and very numerous in from twelve to twenty-four hours, though free bacilli (these are now seen in the cells) have usually disappeared by the end of six or nine hours. In susceptible animals in which the infection is grave and ultimately fatal the number of these cells may increase

up to ninety-six¹ hours. In other cases, however, they begin to diminish on the second day—thirty-six to forty-eight hours—and the numbers fall regularly and steadily until towards the end of the fourth day they become very scanty, though they may not disappear entirely until about the seventh day. Many of these leucocytes appear to undergo rapid disintegration outside the cells, but a certain number of them are ingested by the macrophagocytes (§ 211). This

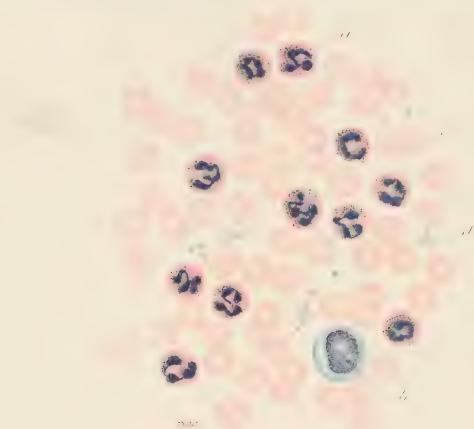


FIG. 6.—Blood film from a case of septicæmia, stained by Leishman's method. ($\times 600$.)

- a.* Polymorpho-nuclear cells greatly increased in number. Marked evidence of leucocytosis.
- b.* Mononuclear hyaline cell. Myelocyte.
- c.* Red blood corpuscles or hæmatocytes.
- d.* Blood platelets.

description may be taken as applying to these cells as they are present around the vessels in most cases of acute inflammation.

Scott points out that immature non-amœboid cells—*myelocytes*—of this type, $14\ \mu$ down to $9\ \mu$ in diameter, with large rounded or oval non-lobulated eccentric nuclei, two-thirds the size of the cell, may sometimes be met with in the blood, for example, in anæmias, in myelogenous leukæmias, and in appendicitis (usually the day before a relapse), and always in the bone marrow. In them the nucleus is not so deeply stained, the reticulum and the nuclear membrane are not so prominent,

the former in some cases being represented merely by a few dark chromatin patches and dots. Mitotic division of the nucleus may occur. The granules at this stage are very fine, and may give a distinct violet or neutrophile reaction.

209. A second granular cell is the *coarsely granular, oxyphile, or eosinophile cell*. It is somewhat larger than the polymorpho-nuclear



FIG. 7.—Blood film showing marked eosinophilia from a case of ancylostomiasis, stained with methylene-blue and eosin. ($\times 600$.)

- a. Numerous coarsely granular eosinophile leucocytes containing Ehrlich's α granules.
- b. Polymorpho-nuclear leucocyte containing ϵ granules.
- c. Mononuclear hyaline cell.
- d. Lymphocyte.
- e. Red blood corpuscles.

cell, and differs from that cell in other essential features. It is usually somewhat ovoid in form, measuring about 12 or 13 μ in one axis and 9 or 10 μ in the other. The nucleus, occupying a relatively smaller proportion of the cell, rarely central and often very eccentric, may be merely a rod with enlarged and clubbed ends, this rod being bent on itself in the form of a horse-shoe or the letter "S"; or again it may be broken up into a series of three or four lobules united by delicate chromatin filaments. The nucleus as a whole is more lightly

stained by the basic anilin dyes than is the nucleus of the polymorphonuclear cell; this applies also both to the nodal points of the chromatin reticulum and the nuclear membrane, which are finer and more delicate, though they are more deeply stained than is the inter-reticular nuclear substance.

The cytoplasm, often considerable in quantity, transparent, and unstained, contains a number of large highly refractile granules, many of them of considerable size— 0.25 to 0.5μ in diameter—though some of them may be much smaller. With eosin and the other acid anilin red dyes these granules, which appear to be most numerous towards the periphery of the cell, are stained very deeply—a clear red or rose pink.

This cell is fairly abundant in the coelomic fluid, in the lymph spaces, in the connective tissues, and in bone marrow, but is not very numerous in the blood, seldom being present in a greater proportion than 2 to 4 per cent. of the whole of the leucocytes. It is amœboid but non-phagocytic. Such cells may be present in small numbers in the fluid taken from the peritoneal cavity of a guinea-pig four and a half hours after it has been injected with *Bacillus coli communis*, the numbers continuing to rise up to the end of twenty-four hours; there is then a gradual fall until the seventh day, when the cells may disappear. It has been claimed that the large eosinophile granules exert an extra-cellular digestive power, but this is not as yet generally accepted. In certain parasitic diseases this form of cell may be present in the blood in large numbers.

The immature form of this cell, the *coarsely granular myelocyte*, is somewhat larger than the fully developed cell—it may reach a diameter of 16μ ; the nucleus is rounded or oval, is very lightly stained by basic stains, and the chromatin reticulum and the nuclear membrane are very ill defined. The granules, small and large, already give an oxyphile reaction, though not so distinctly as at a later stage of their development; mitosis may be observed. These cells occur in small numbers in myelogenous leukæmia, and in parasitic diseases, such as anchylostomiasis, tape-worm disease, etc.

210. The *lymphocyte*, which is sometimes spoken of as the immature leucocyte, is characterised by its small size— 6 to 8.5μ , the size of a red blood corpuscle—its comparatively large and distinctly stained nucleus, and the small amount of faintly stained (basophile) cytoplasm, which may form a crescentic layer on one side of the nucleus, to be continued

as little more than a thin line; or, again, the cytoplasm may surround its nucleus as a somewhat scanty ring or envelope, which in some cases is slightly "spiked" or crenated, and with acid fuchsin and picric acid may show distinct granules. The cell itself is rounded or oval, and the nucleus has usually the same contour, sometimes with a notch or depression at one side; this may represent the initial stage of the formation of a kidney-shaped nucleus. The nucleus is often much more deeply stained than is the cytoplasm, this being due to the intensity with which the nodal points of the chromatin network and the nuclear membrane are stained by basic anilin stains. Sometimes, however, the nuclear staining is not so deep as is that of the cytoplasm. These cells are practically indistinguishable from the small cellular elements that are found in the spleen and in the reticular spaces of lymphoid tissue, though, by some, it is maintained that in this latter position the average size of the lymphocytes is smaller than that of those found in the blood, and that this is due to the smaller amount of cytoplasm present, usually on one side only of the nucleus. These cells are as widespread in the tissues as is lymphoid tissue itself; in the blood they constitute about 25 to 30 per cent. of the leucocytes present. In inflamed areas they may be present in considerable numbers, being brought up apparently along the lymph channels rather than by the blood vessels. Where there is little cytoplasm this cell appears to have very little amœboid activity, but under certain conditions, *i.e.* in those cells in which the nucleus is kidney-shaped or even lobed, and in which the zone of protoplasm is thicker, amœboid activity may be present. Indeed it is evident from a study of pigmented glands, that these cells sometimes assume a phagocytic activity, as small granules of pigment may be seen within a few of even the most characteristic of the cells. Lymphocytes are found in the blood in increased numbers after food is taken, and they appear to be diminished during starvation.

Many of these cells are said to make their appearance in the cellular contents of artificially inflamed tissues at a somewhat later date than do the large hyaline cells, but I have noted that they may be present in considerable numbers very shortly after the polymorphonuclear cells have passed out from the vessels. In all cases they appear to form the larger proportion of the hyaline cells at the later stages of the inflammatory process. Certain cells of this type, which closely resemble the lymphocyte, but have around the nucleus a larger

quantity of spongy and finely granular protoplasm in which vacuoles can often be made out, were first described by Unna, especially in certain inflammatory conditions of the skin. They appear to be associated directly with repair. Certain observers maintain that they are tissue lymphocytes as distinguished from the lymphocytes circulating in the blood. Larger cells of this type are the typical plasma cells of Unna (§ 212).

The lymphocytes are sometimes divided into large and small varieties, the larger forming a kind of intermediate stage, both as regards amount of cytoplasm and depth of stain of the nucleus, between the smaller lymphocyte and the large hyaline cell or mononuclear macrophage described below. For the present, however, we may describe them as distinct forms.

211. The *hyaline cell*, usually the largest of the group, is two or three times the size of a red blood corpuscle. It is oval or rounded or may have a somewhat irregular outline. The nucleus is, usually, rounded or kidney-shaped, and, in the latter case, has its convexity close to one side of the cell of which it constitutes about two-thirds. It is not very deeply stained by the basic anilin dyes, but the fine chromatin network and the nuclear membrane are somewhat more deeply tinted, never so deeply, however, as in the nucleus of the lymphocyte. This nucleus is surrounded by a broad zone of hyaline, non-granular very delicately stained protoplasm. The cell is actively amœboid and distinctly phagocytic. Metchnikoff speaks of it as a macrophage or macrophagocyte. It does not appear to come into action so quickly as does the microphage, but it continues its work long after that cell has ceased to be actively "ingestive"; indeed, it devours not only these microphages with their contents, but red blood corpuscles, protozoal (hæmatozoal) parasites, and bacteria, indiscriminately, when once it gets to work.

The hyaline cell is a comparatively rare cell in the blood, constituting only from 2 to, at most, 6 per cent. of the leucocytes found in normal blood, but it is found in considerable numbers in the lymph spaces of the fixed connective tissues and in the serous cavities where the serous membrane is irritated. Its presence in inflamed areas affords evidence of proliferation of fixed endothelial cells in blood vessels or lining the connective tissue spaces. We have further proof of this in the fact that in such positions, mitotic division of the nucleus

of these cells may often be made out. Whether or not the hyaline cells of the blood are derived from the endothelial or fixed cells by a process of proliferation is still a matter in dispute.

In the artificially induced inflammation of the peritoneal cavity above described these large mononuclear cells appear as early as three hours after inoculation, continuing to increase until, in twenty-four hours, they are fairly numerous. They gradually come to outnumber the polymorpho-nuclear cells until on the third or fourth day they, with the lymphocytes, constitute the whole of the new cells present. This increase may go on to the eighth or ninth day, and the decrease in number of the polymorpho-nuclear cells appears to result from the powerful phagocytic action of these mononuclear cells which ingest them in large numbers.

Scott has described an *immature* form of this cell—the *hyaline myelocyte*—usually $10\ \mu$ to $12\ \mu$ in diameter, which appears to be distinct both from the immature form of the lymphocyte, and from the lymphocyte itself. Its “nucleus fills three-quarters of the cell, is smooth, round or oval” and “pale, often containing only two or three chromatin patches, and is then paler than the surrounding protoplasm. In deeply stained films an incomplete network and a fine nuclear membrane may be seen. The protoplasm is basophile, stains homogeneously, and has the opaque appearance of ground glass. Mitosis occurs and karyokinesis is sometimes seen.” This form is rarely found in the blood except in cases of myelogenous leukaemia and other diseases in which the bone marrow is involved; but in normal bone marrow it, along with all the immature forms above described, except the lymphocyte, which more often affects the lymphoid tissue, is found. Mitosis may be seen in these cells.

212. Plasma cell of Unna.—This cell is essentially a rounded, ovoid, angular, or slightly irregular mass of spongy or finely granular, vacuolated protoplasm surrounding a nucleus, which is usually placed eccentrically and lies in a definite clear space—probably a more delicately stained protoplasm. This space is seen in most of the mononucleated rounded cells, but never so distinctly as in the plasma cell, in which it forms a kind of “court” around the nucleus. The nucleus is described as “wheel-like,” from the fact that on the inner sides of the distinct nuclear membrane are apposed little masses of nuclear substances (the rim) from which thin threads or strands

(corresponding to spokes) run to join a central mass of chromatin (the hub). These plasma cells are described by Unna as occurring especially in certain inflammatory conditions of the skin, but they appear to be associated with other conditions in which there is irritation of the connective tissue cells, especially of those in the immediate neighbourhood of blood vessels as in chronic inflammation and around advancing tumours. It is probable that although these cells, as usually seen in slowly fixed tissues, are rounded, the spongy and granular protoplasm in rapidly fixed plasma cells sends out short thick irregular processes.

Stain (§§ 160, 161, and 162). The protoplasm takes on the blue tint somewhat deeply, but a number of more deeply stained granules stand out very distinctly from the background, the wheel-shaped nucleus, with a clear space surrounding it, is also distinctly seen.

Stain (§ 164). Here the protoplasm is of a brownish-grey, whilst standing out from this background numerous brick-red granules differently arranged may be seen distinctly. Use also Victor Bonney's stain (§ 150).

These plasma cells are contained in rounded or angular spaces between the fibrils of the connective tissue, and are not continuous with one another except just as they are undergoing division. They appear to have no direct relation to the formation of the fibrillar tissue itself, although they are so closely connected with it. Maximow, who has studied these cells somewhat carefully, considers that the plasma cell along with the mononuclear cells, the lymphocyte, and certain other cells in which the chromatin of the nucleus is specially prominent and deeply stained, but in which the space surrounding the nucleus, though present, is not so distinctly seen and the wheel-shaped nucleus is not seen, may be classified under one heading as "polyblasts," or cells that under different conditions assume a variety of forms. Under ordinary conditions they play no part in the formation of collagenous or fibrillar tissue; they appear to be distinct not only from the polymorpho-nuclear cells on the one hand and from the fibroblasts on the other, but also from the endothelial cells from which blood vessels are developed. They play a part, however, in preparing the way and maintaining the nutrition of the fibroblasts and endothelial cells in fibrin, in foreign bodies, etc., in which, ultimately, vascularisation and cicatrization are found.

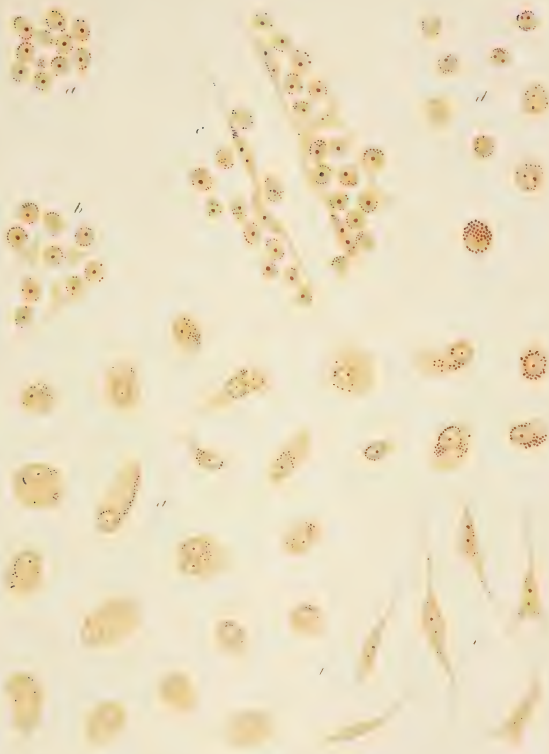


FIG. 8.—Cells from sections stained by Beckton's method. ($\times 800$.)

- a. Group of lymphocytes from a lymphatic gland.
- b. A small portion of a patch of lymphoid tissue from the vermiform appendix.
- c. Lymphoid tissue from a section of a tonsil, showing a lymphatic vessel.
- d. A group of five lymphocytes, two "hyaline" or large mononuclear cells, one polymorpho-nuclear leucocyte and an eosinophile cell.
- e. A group of four fibroblasts.
- f. Two endothelial cells from the wall of a small blood vessel.
- g. Plasma cells from various sources. Inflamed appendix, fibro-adenoma of breast, carcinomata (of tongue, skin, breast, and cervix uteri).

213. The *basophile cell*, which appears to be related to the granular "mast" cell that is found in the connective tissues during the process of inflammation, is about the size of the polymorpho-nuclear cell—sometimes a little larger, though the mast cell is said to be smaller than the polymorpho-nuclear cell. Its nucleus, faintly stained, consists of several lobules united by narrow bands of nuclear substance. The chromatin network and nuclear membrane are not well defined, but can usually be distinguished. The transparent protoplasm remains unstained, but embedded in it are granules which vary much in number and size and sometimes in staining. In some cases they are very numerous and large, measuring as much as 0.5μ in diameter. In such cases it is difficult to make out the outlines of the nucleus, which is almost hidden by the large deeply stained granules closely packed together. Again, most of the granules may be very small, with a few large granules scattered at wide intervals; the nucleus is then not nearly so much obscured. The large granules take on the basic dyes strongly, and are stained a deep violet blue or purple; the smaller stain less intensely and may not be quite so distinctly basophile. In the *immature* cell the rounded or oval nucleus is relatively small; it is not lobulated, stains very faintly, and shows little structural detail. The granules are usually of the larger type, and take on the characteristic basic stain. Few of the fully developed basophile cells with the larger granules are found in healthy human blood—0.5 per cent. of all the leucocytes—but in the connective tissue spaces they are found, sometimes in considerable numbers. These cells are non-phagocytic and non-amœboid. Like the other granular cells of the blood, they appear to be formed specially in the bone marrow, where the immature forms are often present, and where the various gradations up to the mature forms may usually be seen. In cases of myelogenous leukæmia these basophile cells, especially the immature forms, may be fairly numerous. The cells containing the finer basophile granules may be found in normal blood, but comparatively rarely. It should be noted that in this form, which has been said to correspond to the mast cell, the nucleus is often trilobed and the amount of protoplasm small (Pappenheim). An interesting point in connection with this cell and its suggested relation to the lymphocyte is that it, like this latter cell, is found in the blood in increased numbers after meals. Moreover, when stained by Unna's polychrome methylene-blue (§ 160) the granules are blue.

MAST CELLS

214. Stain (§§ 122, 158, and 160). The best stain for mast cells is thionin. These cells when stained with a neutral mixture of acid and basic dyes are seen to contain granules more basophile than the nucleus. These granules, Ehrlich's γ -granules, are distinctly metachromatic, taking on a red stain and standing out very prominently from a blue or violet background when the violet basic anilin dyes are used, and assuming a yellow tint with most of the red basic dyes, thus resembling mucin and pseudomucin.

The granules of the mast cells present in the blood in myelogenous leukæmia appear to be very soluble in water, and cannot be demonstrated when water has been used in the preparation of the cells. The mast cells found in the connective tissues resemble those met with in the blood, though in the latter case the granules are not so distinctly metachromatic. Mast cells are met with in the various inflammations of the skin, especially those of specific origin, in epithelial tumours, in syphilitic inflammations of the skin, mucous membranes, and other tissues, in keloids in scars, in peripheral neuritis, in the walls of the vessels of the cerebral cortex in progressive paralysis, in the lungs in brown induration, in the various exudates, and in the blood of leukæmic patients, in the connective tissue, and in the bone marrow. They measure from 6 or 7 μ to 15 μ or more in diameter, and vary greatly in shape, some being rounded almost like lymphocytes and hyaline mononucleated cells, others larger and oval, others again almost spindle-shaped or with many branching processes. When met with in the connective tissues the nucleus is single, rounded or ovoid, unlike that of the basophile cell of the blood in which the nucleus may be lobed. The most marked characteristics of these cells are the γ granules of Ehrlich, who looks upon them as the result of some special cell metabolism or over-absorption. Mast cells, however, must be associated with post-embryonic and full developmental periods of cell activity, for they appear to be most numerous in the later periods of life—during the periods of activity of the fully formed connective tissue, especially of the skin, of the bone marrow, and of the cells within lymph spaces.

215. Many authors describe what are called *transitional cells*. These, apparently, correspond to the various immature cells above described.

They are characterised by slight indentation of the nucleus and a faintly granular protoplasm. They are probably developmental stages in the life-history of the more typical granular cells.

216. Great stress is laid by Ehrlich, Unna, Pappenheim, Schridde, and others upon the character and staining of the granules met with in various blood and tissue cells. Most of these granules may be included in Ehrlich's classification.

Eosinophile, acidophile, oxyphile, or α -granules which take up the acid dye from any mixture of acid, neutral and basic dyes. These are best seen in the coarsely granular oxyphile cell of the blood and tissues.

Amphophile or β -granules stain with both acid and basic anilin dyes, and are probably seen best in the blood of certain animals, *e.g.* the rabbit.

Basophile or γ -granules stained by basic dyes, are seen in the basophile cell of the connective tissues.

Small basophile, or δ -granules, which stain with basic dyes only, are found in certain mononuclear cells—plasma cells.

Neutrophile or ϵ -granules stain with neutral dyes. They are found in the finely granular polymorpho-nuclear cells, they are said to correspond to the pseudo-eosinophile granules of the lower animals, and differ from the eosinophile granule in that they are considerably smaller and give a less distinctly acid reaction.

Various shades of red, blue, and violet may be brought out in these granules by the use of polychrome methylene-blue, and other mixtures of different acid, neutral, and basic dyes.

Iodophile granules. — Stain (§ 133*a*). In acute pneumonia, leukæmia, erysipelas, scarlet fever, septicæmia, acute phthisis and other diseases, a certain number—as many as 25 per cent. of the polymorpho-nuclear leucocytes—may take on a diffuse brown stain; or coarse deeply stained brown or port-wine coloured granules may be seen scattered through the protoplasm; or similar granules may be found accumulating at the periphery of the cell. These do not correspond to the neutrophile granules, and give a definite iodine reaction. Similar granules are said to occur in the cells present in myelogenous leukæmia, and it is recorded that they are also present in the mononuclear cells under similar conditions, but the cells specially affected are undoubtedly the polymorpho-nuclear leucocytes.

217. *Blood platelets*.—If a drop of a solution made up of equal parts of 2 per cent. solution of common salt and a glycerin dahlia solution (Russell and Brodie), or of Kemp and Calhoun's fluid,

Formalin	50 parts,
Sodium chloride	10 „
Methyl-violet	1 part,
Water	100 parts,

be placed on the skin at the side, or at the root, of the finger-nail, and a puncture be made at this point so that the blood may flow directly

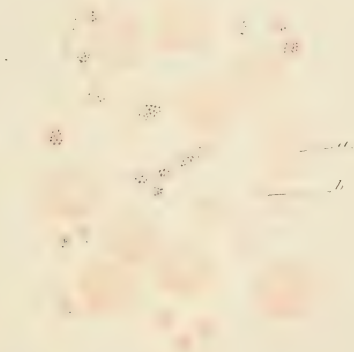


FIG. 9.—Red blood corpuscles and blood platelets stained with eosin and methylene-blue. ($\times 1500$.)

a. Red blood corpuscle.

b. Blood platelets.

into and mix with the fluid, the resulting mixture taken on to a clean slide is found to contain a number of delicately stained (purple or blue) circular or ovoid corpuscles, $2.5-3.5 \mu$ in diameter; they have no nucleus, and their protoplasm is finely granular. They are present in the proportion of about 1 to 10-28 of the leucocytes, *i.e.* 180,000 to 500,000 per cubic millimetre of blood. When blood is allowed to flow from a cut blood vessel these corpuscles are seen to accumulate in large numbers at the point where the blood leaves the vessel. If a drop of blood be examined at once ($\times 800$) the platelets may be seen for a few seconds, but they soon disappear, apparently forming points from which strands of fibrin radiate. In blood rapidly fixed and stained with eosin

and methylene-blue, the platelets have the appearance presented in Fig. 9.

It is interesting to note that these corpuscles are usually increased in number in all conditions in which there is evidence of an attempt at regeneration of blood, for example, following hæmorrhages and in myelogenous leukæmia. They are diminished in number where blood poisons are given or formed—as in certain fevers. During the febrile stages of malaria they may disappear, only to reappear and increase in numbers after the fall of the temperature. They should be studied carefully in relation to the clotting of the blood.

ENDOTHELIAL CELLS

218. To see endothelial cells, a healing wound, an old pleurisy or pericarditis, or an embryonic blood vessel may be examined. Harden (§ 58 or 59). Stain (§ 162).

($\times 50$ and $\times 1000$).—Note double rows of spindle-shaped sections of cells somewhat like the fully developed fibroblasts already described, the more elongated nucleus stained green with its deeply red pyronin stained nucleoli, stands out prominently from the red, finely granular cell plasm, which appears to be somewhat more scanty than in the case of the fibroblast (Fig. 20). Stain (§ 164). The red granules are neither so large nor so numerous as in the cytoplasm of the fibroblasts. There is no branching of these endothelial cells, and little evidence that they lay down any definite periplast. It may be that they are simply modified forms of the fibroblast in one direction, as the mononucleated cells, large and small, are held to be modifications in another.

FIBROBLASTS

219. Examine ($\times 50$) any stimulated connective tissue—say from the floor of an ulcer (Figs. 18 and 20). Note the branching cells, the protoplasm of which is stained red with pyronin, the nuclei green.

($\times 700$ or $\times 1000$).—The protoplasm of these cells is seen to be granular or spongy-looking, sometimes vacuolated. This protoplasm may send out numerous processes some of which are distinctly branching, or it may be collected into a spindle-shaped mass surrounding an elongated nucleus, which is very delicately stained, the reticular strands being very fine and the nodal points small. The nuclear mem-

brane though thin is quite evident. In certain cases the nucleus is undergoing mitotic division, the cell in this case losing its elongated form and the processes becoming shorter and less distinct. The older cells lying between the fibrillar or collagenous tissue are distinctly spindle-shaped; the nucleus then takes on an even lighter green stain, but the nucleoli stand out distinctly as red pyronin stained points. These cells may be 40 or 50 μ in length and from 3 to 5 μ in breadth. The older cells, seen in section, resemble the endothelial cells (§ 218), except that the nucleus is surrounded by a larger body of cytoplasm. Moreover, there is, as a rule, no continuity between the processes of adjacent individual cells such as almost invariably exists between the endothelial cells. Stain (§ 164). The nuclei of these cells are left almost unstained, but the paired nucleoli stand out very distinctly, the protoplasm of the cell being dotted with small red granules in a very typical fashion.

The protoplasm of the young fibroblasts is much more delicate and spongy than in the older fibroblasts, in which it is denser and more homogeneous, especially at the margins of the cell; according to some observers it is distinctly fibrillated. These cells may, under the action of certain powerful irritants, as in the course of an inflammatory process or when abundant nutrient material is supplied, become swollen, and dividing, may give rise, by a process of proliferation, to a number of more or less rounded hyaline-looking cells, but in most cases the cell appears to send out a long process or extension of protoplasm carrying into or along with it a nucleus derived from the parent nucleus. In such cases the elongated form is not departed from even during the process of proliferation.

220. Maximow classifies the cells that play a part in inflammation and repair into—

(1) Polymorpho-nuclear leucocytes which are brought up immediately by the blood vessels in the early stages of inflammation, cells which are early and actively phagocytic especially in septic conditions, which supply certain of the elements of fibrin, and which also help to prepare the way for the advance of endothelial cells and fibroblasts. Polynuclear leucocytes probably never develop into fixed connective tissue cells. They are removed or broken down at a very early stage of the processes of inflammation and repair, those that remain wandering back to the blood channels.

(2) The polyblasts, including the various groups of cells already mentioned (§§ 208 and 210–214), continue the removal of unnecessary tissue, of fibrin and even of foreign bodies, by a process of active phagocytosis, but which, whilst doing this, along with the fibrin and leucocytes, form a scaffolding and a pabulum into which (3) the (*a*) new endothelial cells (from which are formed the advancing blood vessels) and the (*b*) specially differentiated fibroblasts may make their way, and on which these latter may depend, temporarily, for their nutrition.

INFLAMMATION OF THE OMENTUM

221. The most convenient structure in which to examine the earlier processes of inflammation is the omentum—a typical serous membrane. This is a transparent membrane composed of (1) delicate connective tissue fibrils, and (2) connective tissue cells. It contains also (3) a few elastic fibres, and is traversed by a network of (4) vascular and lymphatic channels and spaces. The membrane is completed by an investing layer of (5) flattened endothelial cells similar to those met with on other serous surfaces. Between these cells are small orifices or stomata, by which a free communication is maintained between the large serous peritoneal cavity (which may be looked upon as a large lymphatic space), and the smaller lymph spaces and channels in the substance of the omentum itself.

To the naked eye the appearances are those presented in inflammation of any serous surface (see § 222). In the very early stages there is simply a rosy flush of the membrane, which is accompanied by a loss of the characteristic glistening appearance of a healthy serous surface. This is due to the presence of exceedingly minute projections, some caused by the distension of the blood vessels, others by minute accumulations of proliferating cells or small patches of coagulated extravasated lymph. Later, the amount of lymph plasma thrown out may become so great that a layer of soft fibrinous lymph is deposited on the free surface.

In this transparent vascular membrane the changes that take place both in and around the vessels and in the fixed tissues may be readily followed, although the inflamed membrane becomes somewhat swollen, succulent, and more opaque. In a case of acute peritonitis, as soon after death as possible (as the endothelial cells, by a kind of post-mortem maceration, are very quickly separated from their trabeculae),

cut out with a pair of fine sharp-pointed scissors a thin piece from the mesentery, or better still from the omentum, spread it out on a slide, stain (§ 102 or 103), and mount in a drop of glycerin (§ 194); cement (§ 201). If the specimen cannot be mounted at once, transfer to Müller's fluid, diluted to one-half the ordinary strength (§ 62), gradually increase the proportion of Müller's fluid for a few days, and then keep in preserving fluid (§ 90), mount and treat as above, or as in §§ 110 (*b*), 199, or 115 and 195 or 199.

In a piece of such a membrane taken from a patient who has died during the early stage of inflammation, the following appearances may be noted.

($\times 50$).—There is (1) marked distension of the small vessels, especially of the venules. Although the distending mass consists mainly of red blood corpuscles, there is in it a larger proportion than usual of stained (white) blood corpuscles. (2) Around the distended venules is an accumulation of leucocytes and lymphocytes, evidently the result of migration; this is best seen at the points where the capillary or small venules open into the larger venules, the migrated cells collecting in the angles at their junction. (3) The endothelial cells, some of which are still adhering to the connective tissue or fibrous trabeculæ, others lying free in the trabecular spaces, appear to be more prominent and more numerous than in the normal peritoneum. In consequence of the rapid proliferation that is going on, many of these cells are smaller than normal, but in the very early stages some of them are greatly increased in size, whilst others appear to be separated from their bed by the rapid effusion of fluids beneath them (the fluid elements that pass out from the distended vessels may be much increased in amount); these, however, are still of considerable size, and retain much of their normal contour and appearance. (4) The connective tissue, or fixed, cells that lie on the delicate fibrillar stroma are seen to be undergoing rapid proliferation.

($\times 300$).—The distended vessels are now readily enough demonstrated, the venules being surrounded by a large number of polymorpho-nuclear leucocytes, which can only have escaped from the engorged vessels, and a few lymphocytes which appear to have come up by the lymphatics. There is also evidence of increased activity of the endothelial cells, many of which are swollen and are undergoing rapid proliferation. Little groups of very regularly shaped cells, or single cells, are seen lying in the spaces of the network; some of these

cells are elongated, others are pear-shaped, whilst others again are irregularly rounded, most of them staining deeply and presenting evidence of rapid proliferation. These cells appear to be derived

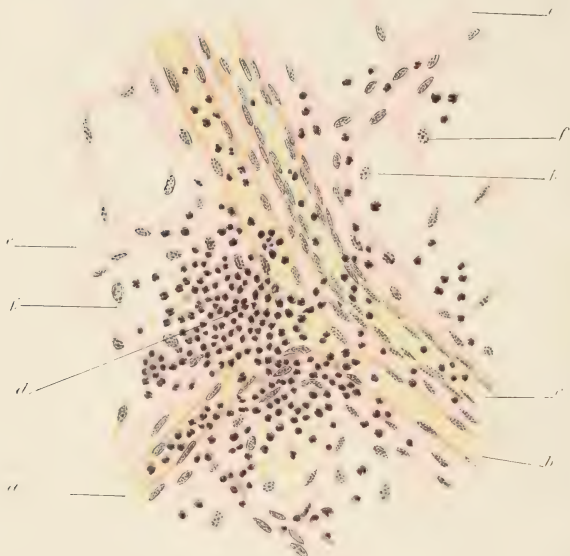


FIG. 10.—Early inflammation of the peritoneum—omentum—taken shortly after death. Stained with alum hæmatein and picro-erythrosin. ($\times 200$.)

- a.* Capillary vein.
- b.* Larger venule.
- c.* Larger arteriole.
- d.* Accumulation of polymorpho-nuclear leucocytes at the angle formed at the junction of *a* and *b*.
- e.* Fibrous trabeculae of the peritoneum.
- f.* Swollen endothelial cells detached from fibrous trabeculae; as yet there is little evidence of proliferation.

from the endothelial cells that cover the network and form the serous surface; some of the larger endothelial cells bulging from the trabeculae are multinucleated, whilst others appear to be undergoing degenerative (especially fatty) changes. It should be observed that certain cells

are contained within the lymph spaces, into which they appear to have made their way by the channels by which they and the fluids ordinarily pass from the vessels into the lymphatics; this, of course, does not apply to certain of the rounded hyaline cells which appear to be derived from the fixed connective tissue cells and lining endothelial cells; though here, again, we may assume, from what may be observed in our specimen, that the proliferative changes are merely an exaggeration of the normal processes of multiplication and regeneration of the cells. In the earlier stages, as here examined, the cells of the connective tissue are comparatively few in number. In the later stages of inflammation, where there is great exudation of lymph, or where organisation has taken place, the microscopic appearances are very similar to those met with on any other inflamed serous membrane (such as the pleura or pericardium) (§ 222).

Now examine a section through a piece of "matted" inflamed omentum. From a case of peritonitis in which there is marked fibrinous effusion, excise a small piece of the matted membrane, fix (§ 59 or 63), harden (§ 60), stain (§ 102, 103, or 104), clear (§ 193), and mount (§ 199).

($\times 50$).—The outlines of the convoluted omentum, cemented together by the plastic fibrin into a solid mass, may be traced. In the omentum itself the fat cells and the distended blood vessels can be readily seen. Around some of the vessels the emigrated polymorpho-nuclear leucocytes, lymphocytes, and pseudo-lymphocytes have accumulated in considerable numbers. The fibrillar tissue on the surface of the omentum from which the endothelium is mostly detached, and forming a kind of basement membrane, is somewhat swollen. Strands of fibrin are to be seen between the folds of the omentum, and in this fibrin are embedded numerous polymorpho-nuclear leucocytes, the nuclei of which are stained deeply by the hæmatein. A number of somewhat larger cells, evidently proliferating or detached swollen endothelial cells, may be seen lying near the swollen fibrillar tissue above described.

($\times 300$).—The distended vessels stand out prominently. The fibrillar tissue of the omentum is evidently somewhat swollen, and here and there in the lymph spaces are polymorpho-nuclear leucocytes and a few lymphocytes. Between the folds of the omentum the delicate fibrinous reticulum is easily made out, and embedded in it are numerous polymorpho-nuclear leucocytes, and a number of cells with a comparatively delicately-stained nucleus and a large amount of

protoplasm, cells which in appearance correspond closely to the hyaline cells of the blood. In one or two instances these cells contain several distinct and separate nuclei. In some places the flattened endothelial cells of the peritoneal surface may be seen to



FIG. 11.—Section of matted inflamed omentum. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- a.* Serous surface of omentum with underlying fibrous trabeculae.
- b.* Fat cells.
- c.* Small blood vessels.
- d.* Fibrinous lymph in which are embedded many polymorphonuclear leucocytes. Near the peritoneal surface swollen and proliferating endothelial cells are present but cannot be distinguished very easily from the polymorpho-nuclear leucocytes under this magnification.

be almost *in situ*, but detached from the swollen basement membrane. In other cases these endothelial cells are swollen, preparatory to undergoing proliferative change, and some are seen to be dividing and to form cells resembling the hyaline cells of the blood.

For those who wish to follow the process further or more in detail, peritonitis may be produced experimentally in the guinea-pig or in the rabbit. From such a case of thirty-six hours' duration the

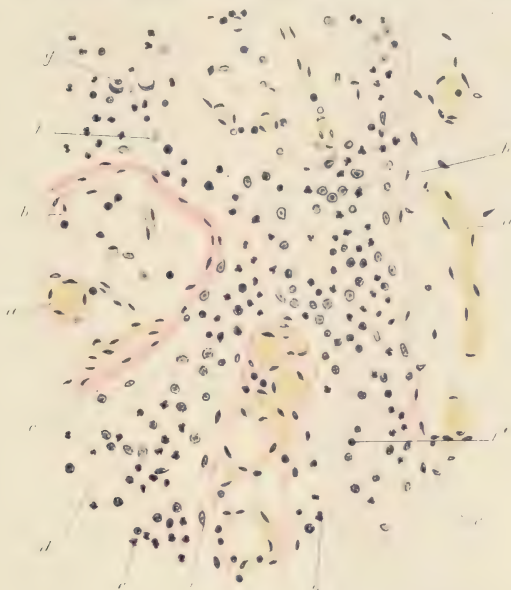


FIG. 12.—Section through matted inflamed omentum. Stained with alum hæmatein and picro-erythrosin. ($\times 200$.)

- a.* Distended blood vessels.
- b.* Fat cells.
- c.* Fibrous tissue beneath endothelial layer of peritoneum.
- d.* Coagulated fibrin on surface of peritoneal surface.
- e.* Polymorpho-nuclear leucocytes—wandering cells.
- f.* Mononuclear cells.
- g.* Lymphocyte or pseudo-lymphocyte.
- h.* Mononuclear phagocyte containing ingested polymorpho-nuclear leucocytes.
- i.* Proliferating endothelial cells.
- j.* Slightly swollen detached endothelial cells.

specimen represented in Fig. 13 is a good example, and in it all the nuclear figures may be fixed at once (§ 59 or 63). Harden (§ 60), stain (§ 102, 103, 104, or 161), and mount (§ 199).

($\times 500$).—Here the fibrillar trabeculæ on which the endothelial cells are lying may readily be made out as they are considerably swollen from the absorption of fluid. There has evidently been some slight escape of red blood corpuscles from the distended blood vessels, and polymorpho-nuclear leucocytes are present in large numbers. Hyaline cells—the macrophagocytes—are here readily recognised, as

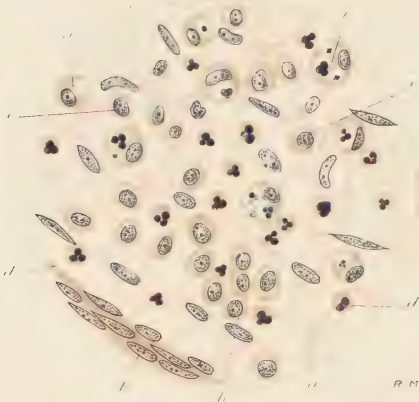


FIG. 13.—Acute inflammation of the omentum, thirty-six hours after an artificial irritant had been applied. Stained with alum hæmæatein and van Gieson's stain. ($\times 500$.)

- a. Fibrillar trabeculæ, swollen as a result of absorption of fluid.
- b. Endothelial cells lying on these trabeculæ, some rounded and proliferating.
- c. Red blood corpuscles.
- d. Polymorpho-nuclear leucocytes.
- e. Mononuclear leucocyte.
- f. Mononuclear phagocyte with ingested polymorpho-nuclear leucocytes.
- g. Ditto with ingested red blood corpuscle.
- h. Endothelial cell of capillary vessel—also (?) fibroblasts.

they have taken into their substance red blood corpuscles and leucocytes; these ingested bodies are usually surrounded by a clear space or digestive vacuole, which may easily be brought out by staining with neutral red (§ 159). In such a case the nucleus of the ingesting cell is pushed to one side and the cell itself is considerably larger according to the number of leucocytes or red corpuscles that it has taken into its substance. Some of these hyaline cells may be

derived from the endothelial covering of the serous surface, others again from the endothelial lining of the capillaries, but most of them appear, at this stage, to come from the circulating blood.

PLEURISY AND PERICARDITIS

222. The series of changes in inflammation of the different serous membranes bear a very striking resemblance in all cases, and much of what has been written in describing peritonitis may be taken as holding good for inflammation of the pleura and of the pericardium. There are, of course, minor differences in structure, not so much of the membrane itself, as of the tissues beneath it, which may, to some extent, modify the appearances of the inflamed surface, just as there may be apparent or superficial differences in wounds healing by first or second intention or by granulation, in spite of the fact that the essential processes are practically identical.

Inflammations of the pleural or pericardial surfaces may be considered in three stages. In *the first stage*, that of congestion, the vessels of the superficial layers of the serous membrane are simply distended with blood so that a rosy flush appears and extends over the surface, the larger vessels being seen tolerably distinctly through the layer of endothelial cells, which even at this early stage are slightly clouded, the glistening appearance being lost. As this is identical with what is seen in early peritonitis (§ 221) it is unnecessary to give any further description of the microscopical changes, except to state that the lymph spaces appear to be increased in size, and to contain a larger amount of fluid and cellular elements than do those in normal tissues. In *the second stage*, during which there is an effusion of serous fluid and coagulable lymph from the congested vessels on to the pleural surface, the changes are more marked; whilst in *the third stage*, where organisation is taking place in this lymph, there is absorption of the fluid, softening and partial absorption of the exuded products, and the formation of new vascularised connective tissue, which gradually takes the place of the fibrin. This process of inflammation (and repair) is usually described as passing through four stages, but for descriptive purposes the above statement is sufficiently accurate.

On naked-eye examination there appears to be little regular sequence, and the appearances vary very considerably in the three stages; but on microscopical examination it will be found that the

course of events is quite definite, the various processes following one another in regular sequence, and, as in the case of a healing wound, varying only according to the amount of fluid or coagulable lymph that is thrown out and the power of the tissues to bring about absorption.

Leaving the first stage as sufficiently described under peritonitis, let us examine the second stage, in which the pleura is cloudy and granular, and the surface dry. On careful examination a thin layer of soft plastic lymph, which can be scraped off with the finger-nail, as a delicate slightly elastic film, may be observed covering the deeply congested surface. On section, the pleura is found to be somewhat thickened and œdematous, whilst the lung tissue immediately beneath may be slightly consolidated; it is always congested. Harden (§ 62 or 63), stain and mount (§§ 102 and 195 or 103 or 104, and 199).

($\times 50$).—If the pleurisy be simple, the changes are observed principally in the superficial or dense layer of the pleura. There is distension of the blood vessels, swelling of the fibrous tissue, and, even at this stage, migrated leucocytes are seen as bright pink or blue points around the turgid blood vessels. On the surface of the pleura is a delicate, almost transparent, layer of fibrin, very unequal in thickness, in which, scattered through its substance, are a few small nuclei (of leucocytes).

($\times 300$).—The dots around the vessels are seen to be stained leucocytes or wandering cells, though even at this early stage a few lymphocytes and hyaline cells with a small number of proliferating connective tissue corpuscles are usually met with. The transparent layer on the surface resembles, very closely, the material that is found in the pulmonary alveoli in acute pneumonia in the stage of red hepatisation, the delicate filaments of fibrin running in all directions and forming a network, in the meshes of which are entangled red blood corpuscles and polymorpho-nuclear leucocytes, sometimes in considerable numbers. This film of lymph is usually thrown out on the endothelial surface, so that beneath the delicate coagulum the swollen endothelial cells may sometimes be seen in profile as spindle-shaped cells with deeply-stained nuclei. Sometimes, however, these cells are detached by the exudation, and are found entangled in the fibrinous lymph, some distance from their original position.

This is all that is to be seen in the case of a simple pleurisy, but pleurisy, it must be remembered, is an almost constant accompaniment of pneumonia. In such a case it is found that the vessels of the deep

layer of the pleura are congested, and that numerous polymorpho-nuclear leucocytes and some lymphocytes or pseudo-lymphocytes are collected around them ; there is also some slight swelling of the bands of fibrous and elastic tissue due to absorption of fluid, so that, in addition to the thickening due to the layer of exuded fibrinous lymph described below, there is always some thickening or swelling of the pleura proper.

When effusion of fluid takes place from the blood vessels into the pleural cavity, there is usually formed a thick soft elastic layer on the pleural surface, which presents a peculiar honeycombed appearance, especially if the quantity of fluid in the serous sac be small. Sanders likened this to the appearance obtained when two slices of bread and butter are pressed together and then separated ; if, on the other hand, fluid is present in considerable quantities, the surface is usually smooth. This layer of lymph may be stripped off as a soft, easily broken membrane, leaving the pleural surface perfectly smooth. A section from such a case is found to present much the same appearance as the specimen above described, except that the fibrinous layer is considerably thicker and more granular looking. It contains a greater number of leucocytes, and is stained somewhat more deeply, often of a peculiar brick-red tinge (with picro-carmin), although it still retains some of its transparency. Around the vessels are numerous migrated leucocytes and proliferated cells ; the lymphatics, which contain a number of leucocytes and lymphocytes, appear to contain, also, granular fibrinous lymph, with which, in a well-stained section, they may be seen to be filled.

In what may be described as *the third stage*, organisation is taking place *in* the lymph which forms a kind of scaffolding on, or in, which new connective tissue is formed, though there is no organisation *of* the lymph itself. The fluid part of the exudation has been absorbed and the two inflamed surfaces having come together are there held, temporarily, by the soft lymph, the lung thus becoming adherent to the wall of the chest. This adhesion may be readily broken down ; it is impossible to detach the whole of the lymph from the pleural surface, though at the points from which it can be detached the surfaces are left rough and irregular, and evidently something more than the original pleura remains. Harden a portion of such a lung (§ 62 or 63) ; stain and mount (§§ 102 and 195 or 103, 104 or 160, and 199).

The organ under consideration was taken from a case in which

the pleurisy was of some standing, and where organisation had commenced in the deeper layer of the lymph.

($\times 50$).—The pleura was much thickened, whilst on the surface was a layer of soft lymph, as described above. In the section we have evidence of considerable congestion of the interalveolar capillaries. The vessels in the wall of the bronchus, and in the interlobular septa, are also filled with blood.

Around these vessels numerous stained nuclei, mostly of polymorpho-nuclear cells, but a few of lymphocytes and hyaline cells, are readily distinguishable. Passing outwards, the pleura is seen to be considerably thickened, and the distinction into two separate layers is in great part lost; the deeper layer appears to be made up of swollen fibres, between which the blood vessels are numerous and are filled with coloured blood corpuscles. The superficial layer is composed of a more delicate nucleated reticular tissue, in which may be seen large sinuses, containing a few coloured blood corpuscles; there are also numerous smaller vessels which appear as loops or branching lines, most of them with their long axes more or less perpendicular to the surface. At certain points these vessels appear to have ruptured, several masses of coloured corpuscles lying free in the young tissue being seen near these cavernous spaces. Above this a layer of cellular tissue, into which vascular loops, recognised as green or yellow lines, bounded by elongated and flattened endothelioid cells, may be seen running perpendicularly or slightly obliquely to the surface. Scattered here and there are a few small brick-red masses, which may be recognised as remnants of altered fibrin. Near the free surface the new tissue is composed almost entirely of granular-looking fibrin. It takes on a deep brick-red colour from the picro-carmin or picro-erythrosin stain, from picro-fuchsin a dull red. Very little light can make its way through this comparatively opaque tissue. Young vessels, in the form of Y-shaped lines, or of more or less perfect loops, may be seen pushing their way from the more fully organised layer into this fibrinous mass; around them in this position are small masses of red blood corpuscles. Between the young vessels, and running along with them, are numerous young connective tissue cells, some rounded, others elongated or spindle-shaped, and forming definite lines. The nuclei of these cells are deeply stained, but it is somewhat difficult to distinguish any protoplasm around the nuclei of the rounder cells under this power. In the brick-red granular lymph which is found

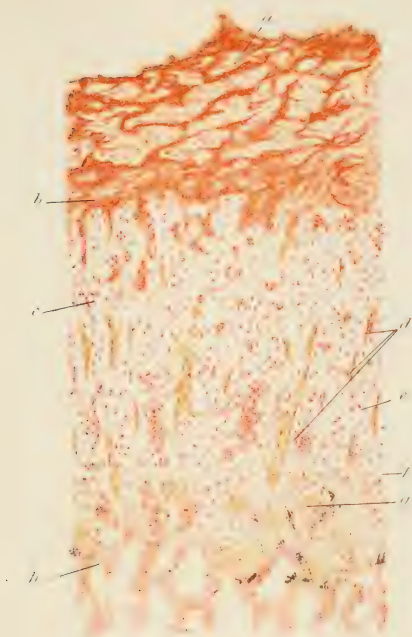


FIG. 14.—Section of thickened inflamed serous membrane (pleurisy).
Stained with picro-carmin. ($\times 50$.)

- a.* Network of fibrinous lymph on the surface, with deeply-stained leucocytes in its meshes.
- b.* Fibrinous lymph in which organisation is commencing.
- c.* Remains of fibrin in organising tissue.
- d.* Newly-formed vessels (vascular loops).
- e.* Larger fibroplastic cells, hyaline, and plasma cells.
- f.* Elastic lamina marking the division between the superficial and deep layers of the pleura.
- g.* Larger well-formed vessels in the deeper layer of the pleura. Pigment in the perivascular and other lymph spaces.
- h.* Lung tissue, somewhat congested. Numerous deeply-stained nuclei (of leucocytes, epithelial cells, and connective tissue cells).

Note the passage of the new vascular loops from the engorged vessels of the thickened deep layer to the organising tissue of the superficial layer.

near the surface, or which remains between the two "granulating" layers, groups of polymorpho-nuclear leucocytes and young connective tissue, hyaline cells, are present, sometimes in considerable numbers. In rare cases a delicate translucent layer of newly-formed fibrinous lymph, like that already described in the second stage, and entangling in its meshes both red blood corpuscles and leucocytes, may be seen.

($\times 300$).—The congestion of the vessels around the air vesicles in the interlobular septa, in the peribronchial tissue, and in the layers of the pleura, is readily made out. These vessels are distended and packed with small greenish corpuscles. Around them the stained migrated leucocytes, lymphocytes, and young connective tissue cells are seen in large numbers; and if these latter are more carefully examined, in one of the interlobular septa, say, some of them are seen to be rounded, others oval, others, again, more or less spindle-shaped. Some are nothing but deeply stained nuclei, others have, in addition to the nucleus, a surrounding mass of protoplasm, and in certain cases this protoplasm is distinctly vacuolated, the "wheel" nucleus being pushed to one side (plasma cells). Where the cell is spindle-shaped, the protoplasm is often slightly fibrillated.

Examine the part of the pleura in which, under the low power, the tissue is most translucent. Here there is evidently a considerable quantity of new connective tissue, and the original deep pleural layer can only be distinguished by the presence of the pigment in the lymphatics. Above this is a delicate, clear, yellow (elastic) wavy line, dividing the deep from the superficial layer of the pleura, the latter of which is gradually lost in the new or organised tissue, which is made up of numerous rounded, branching, or spindle-shaped cells, each with a distinct nucleus. Between these cells is a variable quantity of delicate fibrillated stroma. Towards the deeper part are vessels with relatively thick, well-organised walls, in some of which can be discerned a distinct muscular coat and an endothelial lining. These appear to be the pre-existing vessels of the pleura, which in some instances are considerably dilated, and are almost invariably filled with coloured blood corpuscles (stained green or yellow). Nearer the surface are numerous large rounded or oblong openings, the walls of which are formed of one or several layers of compressed or flattened cells, or nucleated spindle-shaped endothelial cells. Some of these spaces are quite empty, but others, as already seen under the lower power, contain coloured blood corpuscles.

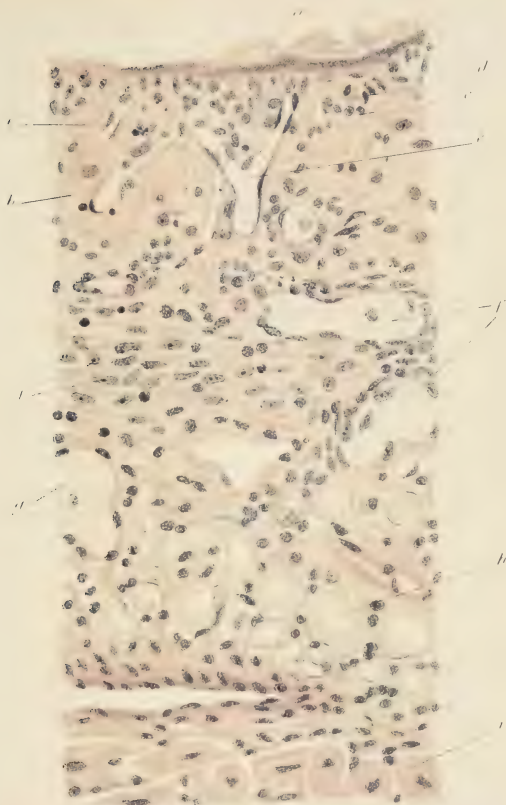


FIG. 15.—Section from case of organising pericarditis stained with logwood and eosin. ($\times 300$.)

a. Thin layer of fibrinous lymph, but little altered, on surface of new membrane. *b.* Altered degenerating fibrinous lymph in which organisation has commenced. *c.* Leucocytes, principally polymorpho-nuclear, emigrated from new vascular loops. *d.* Connective tissue or hyaline cells carried into fibrin along with vascular loops. *e.* Oblique and transverse section of vascular loops, probably derived from the large sinuses (*f* and *g*) immediately below. These are merely the distended, pre-existing blood vessels of the epicardium. *e'*. Small blood vessel, apparently formed from endothelial cells. *h.* Fatty tissue of deep layer of the epicardium. *i.* Muscle fibres of wall of heart. *j.* Layer of well-formed connective tissue cells immediately below the young organising tissue; the passage of connective tissue cells from this into the superjacent fibrinous mass along with the loops of blood vessels is well seen.

The small capillary channels or vessels in the connective tissue are of the very simplest structure. The lumen is bounded on each side by a single or double row of elongated spindle-shaped cells, which may be seen running in various directions; the majority of them run at right angles to the surface, though from the number of transverse branches near the surface it is evident that these capillaries are really in the form of loops, with the convexity of the loop outwards. Between the double row of cells a single row of coloured blood corpuscles may be seen. These capillary loops (Figs. 14, 15, and 16) are in structure much like the vessels found in ordinary granulation tissue, or in the substance of a sarcoma, and, as in those positions, so here, the blood has in some cases made its way from the capillary into the surrounding tissue, the delicate vascular wall yielding to any slight sudden increase of blood pressure. In this specimen small extravasations of blood have occurred near the transverse or superficial parts of the loops.

Under this power, too, examine the lines of spindle-shaped connective tissue-like cells, arranged in two groups, one set passing at right angles, the others parallel to the surface. These rows of the first set are frequently separated by lines of green discs or coloured blood corpuscles, so that they may be looked upon as the cells of which the walls of the young blood vessels running at right angles to the surface are built up, though others of the cells seem to run between the vessels and to be of a more regular connective tissue type. Other cells of the second set are placed with their long axes more or less parallel to the surface; they, also, are spindle-shaped, and have lying between them a clear delicately stained homogeneous material, coagulated fibrin or fibrinous lymph, which, as a rule, presents but little trace of fibrillation. Passing towards the free surface, the fibrinous lymph becomes more noticeable, and is seen as large opaque red granular masses, in which are a few vessels surrounded by a number of more or less rounded cells. In this layer the organisation is at its very earliest stage. The walls of the vessels are of purely embryonic type, and are formed of cells—some of them a little flattened—laid end to end, between which lie the rows of red blood corpuscles. In some parts of the section it is difficult to distinguish any vessel wall; the blood corpuscles appear to be simply pushing their way into the fibrin, but some of the sections of vessels are of considerable size, and are surrounded by both leucocytes and young connective tissue corpuscles in considerable numbers. Near the surface the connective tissue cells are both embryonic and few in

number. On the surface of the opaque red granular mass there is often a layer of lymph of very recent formation, which consists of a network of fibrin similar to that described as present in the air vesicles of the lungs in acute pneumonia, during the stage of red hepatisation. Entangled in this network are a few leucocytes and some small cells

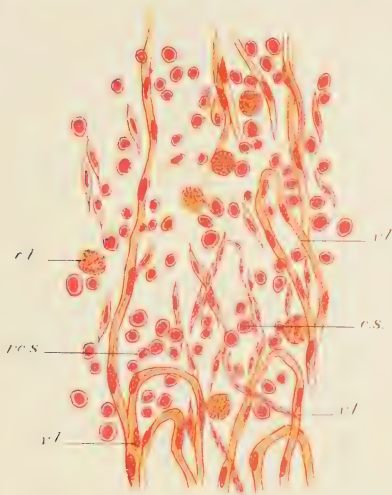


FIG. 16.—Loops of blood vessels in organising tissue on a serous surface. Section stained with picro-carminé. ($\times 300$.)

- v.l.* Loops of vessels fully formed; the structure of these is very readily made out.
- c.s.* Double rows of spindle-shaped connective tissue or endothelial cells, from which the embryonic vessels are formed. Most of these cells are arranged with their long axes at right angles to the surface.
- c.l.* Large cells, very like hyaline cells, met with in all granulation tissue, derived from connective tissue cells.
- r.c.s.* Lymphocytes and pseudo-lymphocytes.
- c.p.* Plasma cell (?).

with single rounded nuclei, though not nearly so many as are found in the air vesicles; there are also numerous red blood corpuscles. This layer has already been described as occurring in a recent pleurisy, so that, here, it has probably been formed some considerable time after the layer in which organisation is now so far advanced.

HEALING OF WOUNDS

223. In describing the healing of wounds it should always be borne in mind that though the process is essentially the same in all cases, the appearances and results are greatly modified according to the loss of tissue; according to the amount of extraneous or temporary supporting material that is thrown into and left in the wound, which for the time may serve as a scaffold, but which afterwards must be absorbed; and, further, according to the amount of stimulation or external irritation. We have, therefore, all intermediate stages between healing by first intention and healing of an ulcerated surface, where, owing to the large gap that has to be filled up by newly-formed tissue, much of which plays a merely temporary part, the processes of disintegration and death of the new tissue go on very rapidly, the formative process, however, always being slightly in the ascendant.

If a clean incision with a sharp knife be made into the soft tissues and the hæmorrhage be allowed to cease, all blood being carefully sponged away before the two cut surfaces are again brought together, and if these surfaces are kept in close apposition by gentle pressure, the wound in the course of a few hours may be so far healed that it requires some little effort to open it up, and in three or four days healing may be almost complete.

In a wound healing directly in this fashion the amount of exuded "lymph" is exceedingly small, only just enough being thrown out to form a glazing over the cut surfaces; this may be seen during about the first twelve hours. There is little distension of the blood vessels, and the surfaces are only slightly redder than normal. If a section (stain (§ 103, 110½, or 160) and mount (§ 199)), including, and made in a plane at right angles to, the two surfaces, be examined, the granular coagulated fibrinous lymph may be readily distinguished as a thin layer in which, even at this stage, especially in the neighbourhood of the distended vessels, a slight increase in the number of leucocytes may be readily enough made out (both $\times 50$ and $\times 300$). Should the specimen be obtained the day after the wound has been made, the number of leucocytes is usually very considerably increased (so much so that to the naked eye the surface has now a regular greyish opaque covering instead of a transparent glaze); there is also evidence of proliferation of the fixed connective tissue cells (hyaline and plasma cells) in the immediate neighbourhood of the incision. The amount of fibrin

is somewhat diminished, and what remains is invaded by leucocytes and larger round cells, the former having escaped from the distended vessels, the latter being derived by proliferation from the connective tissue cells, as already described. Shortly after this all that remains along the line of the incision is a slightly increased number of the various cellular elements; the whole of the fibrin, which first becomes granular, is gradually absorbed, and if the cut epithelial edges have been brought into accurate apposition, the wound may appear to be perfectly healed. This line of new cellular tissue interposed between the original fully formed tissues can, however, be distinguished for at least four or five days after the union is, to the naked eye, complete. It is best seen under the low power, and should be always carefully searched for.

If then the film of coagulated fibrin is merely sufficient to keep the lips of the wound in temporary apposition, the process of organisation goes on under the very best possible conditions; the less tissue there is to be removed by the phagocytic leucocytes, and the less "bridging" the connective tissue cells and the embryonic blood vessels have to do, the shorter will be the time required for the completion of the process of organisation and healing.

224. In a section taken from a healing wound at the end of a stump at about forty-eight hours after amputation, and in which the epithelial covering had, at points, become continuous as a thin blue line, the characteristic processes met with in a wound healing more slowly may be followed. Harden (§ 58), stain and mount (§§ 102 or 103 and 195).

($\times 50$).—At the point where the incision was made the subcutaneous tissue has been partially replaced by a small mass of adipose tissue. At the point of apposition there is considerable infiltration with leucocytes, both at the margin of the corium and at the edge of the fatty tissue. In addition to this, however, there is evidently an increase in the number of proliferating connective tissue cells, with a corresponding, perhaps a preliminary, absorption of fat globules. Deeper down in the line of incision is a space in which a small clot of blood has accumulated between the two apposed margins; near this clot is marked proliferation of the connective tissue cells, lying around which a number of black and golden brown pigment particles are seen. Passing still further down it may again be noted that where the cut

surfaces of the adipose tissue have come together, the fat globules have been absorbed, and that accompanying this is evidently some proliferation of the connective tissue cells; still further down is a mass of blood from which the absorption of the pigment has not yet gone very far, although there is great proliferation of the surrounding connective tissue cells, many of which appear to contain particles of pigment. It may be observed that at the surface the epithelium has grown over a thin film of connective tissue and endothelial cells, which has brought about adhesion of the margins of the wound; the proliferation of the nuclei at the margin of the wound, *i.e.* between the adipose tissue and the outer corium, is very well marked along the whole line of incision, but at one or two points there is an enormous increase in the number of stained nuclei. Wherever these nuclei are in excessive numbers there appears to have been an extravasation of blood, and the fat globules appear to be undergoing absorption.

In many places where, apparently, such extravasation has occurred, tissue composed of elementary capillary vessels and small round cells, the granulation tissue of the surgeon, has taken the place of the fat, and in the cells is a considerable quantity of altered blood pigment; there is also pigment at the margins of some of the fat cells, both where the fat has been invaded by the newly-formed tissue and where it is still comparatively free; in the deeper part, where the extravasation of blood is considerable, the small round-cell tissue around the clot may be very readily made out.

($\times 300$).—The continuous layer of epithelium may now be traced more distinctly as a very thin film forming a delicate bridge across the wound; below this is a thin layer of connective tissue cells, in which, however, it is impossible to distinguish any blood vessels, though distended capillaries run up to its very margin. Beneath this is a sinus of considerable size, apparently part of the incision that has remained unhealed; along each side of the sinus is a mass of adipose tissue, and on one side is an accumulation of leucocytes and lymphocytes lying between the individual fat globules, whilst here and there are larger hyaline cells, some of them apparently proliferating connective tissue cells, with dividing or divided nuclei.

In the corium, at the margins of the incision, we find a similar state of matters, but although the polymorpho-nuclear leucocytes are not so numerous, the larger cells, derived from the connective tissue cells by proliferation, are present in greater numbers, and stand out



FIG. 17.—Deeper part of healing wound taken from a stump forty-eight hours after operation. Stained with logwood and eosin. ($\times 50$.)

a. Leucocytes and proliferated connective tissue cells in the space between the two surfaces which are not brought into accurate apposition; more marked on the right side than on the left. *b.* Part of remaining fissure. *c.* Adipose tissue. *d.* Mass of cellular tissue in which is altered blood pigment. Red cells absorbed and broken down by the leucocytes and connective tissue cells. *d'*. Smaller mass of pigment contained within cells. *e.* Pigmented fat cells. *f.* Other masses of pigment, some free, some within the larger cells. *g.* Altered blood clot surrounded by mass of cellular tissue. This must be absorbed before complete healing can take place; this absorption is carried on by leucocytes and invading connective tissue cells carried in along with the loops of the new blood vessels. Greatest vascularity and most granulation tissue are seen where the apposition is least perfect.

prominently. At the bottom of this sinus the adipose tissue and the fibrous tissue of the corium have met in a line in which the two sets of cells are so blended that it is impossible at first sight to distinguish one from the other. A few small vascular loops are seen running towards this cellular junction, but only one or two small channels can be made out in the mass of cells. Following the line of incision, small but distinct fissures are met with at one or two points; from the presence of these it may be gathered that adhesion is not perfect along the whole line of the incision. This persistence of the fissures is especially well marked in those areas where the fibrous tissue on one side is very dense, and where the increase in the number of the cells appears to be confined entirely to the flap in which the adipose tissue is contained. A little further down where the junction is taking place between two small bands of adipose tissue, the adhesion is perfect; the cells from the two sides are quite indistinguishable, but no blood vessels can be made out in the cellular mass, although no doubt they are present, as they are to be seen in considerable numbers lying between the elements of the fatty tissue in the immediate neighbourhood of the wound. The large spaces in which blood has collected have a very characteristic appearance; they are surrounded by delicate cellular tissue, and in some cases where the blood has been absorbed a mass of granulation tissue has actually taken the place of the blood. In the cells of this granulation tissue and in the surrounding lymph spaces, numerous pigment granules are found. These are usually much darker in colour than the pigment-stained fat cells found in the immediate neighbourhood of the clot or enclosed within the granulation tissue. In some places the remains of the blood clot may still be seen surrounded by the granulation tissue cells, many of which contain a large quantity of pigment, so much, in fact, that it is possible to make out simply a mass of granules with the outline of a cell, none of the protoplasm being stained sufficiently deeply to indicate that we have to deal with a cell. Some of these pigment-containing cells are of large size, and are then much more like the large endothelioid cells, sometimes spoken of as giant cells. Wherever the line of junction is incomplete there appears to be little cell proliferation, at least on one side. Adhesion and organisation take place most rapidly where we have delicate connective or adipose tissue, usually at some little distance away from the surface; large accumulations of coagulated lymph or blood appear to interfere with

this; where this has occurred, the coagulum has all to be absorbed by the polymorpho-nuclear or hyaline leucocytes or by fixed connective tissue cells before the regular organising process can go on. In some parts of the section where fibrinous effusion is reduced to a minimum, all that remains to indicate the position of the healing process, is a thin line of deeply-stained nuclei of leucocytes, of lymphocytes and plasma cells (the more direct the union the fewer of these there are), and of fixed connective tissue cells; it is not always possible, as we have seen, to follow the blood vessels into or through this delicate cell mass, and it appears that organisation may take place without the formation of new vessels if the tissues on the two sides of the wound can be approximated sufficiently closely. At whatever stage these healing wounds are examined we find that, until the granulation tissue becomes well organised, there is usually evidence of vascularisation and of remaining traces of the scaffolding of fibrinous lymph in which the new tissue is formed, so that even in the comparatively late stages of organisation little patches of granular or amorphous matter are seen, brick-red or orange in the specimens stained with picro-carmin, or dirty brown, or reddish-purple, in specimens stained with logwood and some contrast stain. As the healing proceeds and the hæmorrhages are absorbed, the patches of effused blood become more yellow, the pigment being separated from the red blood corpuscles in the degenerating clot by the active phagocytes of the new tissue. It is sometimes held that it is necessary to have a perfectly clean granulation surface in order that the epithelial covering may grow over any healing surface from the margin, but in carefully prepared sections of healing wounds I have very frequently been able to make out the epithelial layer gradually creeping along the granulation tissue, and making its way between this tissue and the layer of fibrinous lymph covering it, dissecting the lymph from the outer granulation tissue. It is also said that the epithelium does not advance until the vascular loops in the granulation tissue have become obliterated, but although this is partially true (for these vessels gradually lose their embryonic character, become fewer in number, and also become better supported), these vessels persist for some time after the wound is closed in by the epithelial covering. It is only later that most of them become obliterated.

The method of formation of these vessels, and the way in which they are obliterated, must be considered after we have examined a healing ulcer, and the organisation in coagulated lymph on other surfaces.



FIG. 18.—Chronic ulcer of leg. Stained with alum haematein and van Gieson's stain. ($\times 300$.)

- a.* Longitudinal section of blood vessel in cedematous granulation tissue.
- b.* Transverse section of ditto.
- c.* Collection of polymorpho-nuclear leucocytes around a new blood vessel.
- d.* Mononuclear cell.
- e.* Fibrillar reticulum, spaces of which are filled with fluid.
- f.* Fibroblast.
- g.* Endothelial lining of blood vessel.
- h.* Plasma cell.
- i.* Lymphocyte (pseudo-lymphocyte).

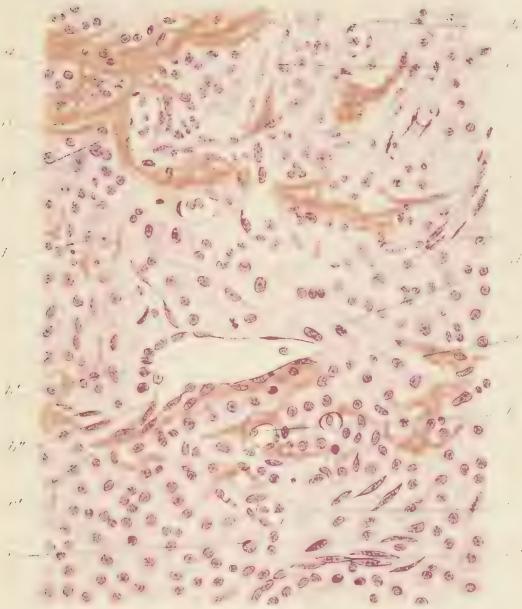


FIG. 19.—Healing wound near surface (three or four days after incision?) Section stained with logwood and eosin. ($\times 400$.)

a.a'.a''. Fibrinous lymph in process of absorption.

b. Small embryonic blood vessel, containing a polymorpho-nuclear leucocyte and surrounded by a primitive perivascular lymph space.

b'. Large vascular space from which smaller vessels (*b''*) open out.

c.c'.c''. Rows of cells indicating the course of new blood vessels. Sometimes these appear to be buds from pre-existing vessels, at others parallel rows of endothelial cells (*c''*) which eventually form definite channels, into which the blood passes.

d. Large connective tissue cells (fibroblasts) from which new tissue is formed.

e. Large connective tissue cell, the nucleus of which is undergoing indirect division, and shows mitotic figures.

f.f'. Polymorpho-nuclear leucocytes and lymphocytes in a blood vessel, and in the connective tissue spaces.

g. Plasma cell.

HEALING ULCER

225. Ulceration usually takes place in tissues of low vitality, especially where there is a tendency to venous engorgement and œdema; it may also occur as the result of injury or over tumours. In these cases there is simply a destructive process, the dead tissue appearing as moist greyish fragments on the irregular, ulcerated surface, on which scattered hæmorrhages occur. The characteristic features of such an ulcerated surface are loss of tissue and the presence of dirty grey, sloughing patches, some of which may be seen to be separating from the tissue beneath them. There is often great œdema in the surrounding tissues, so that the loss of substance usually appears to be greater than it actually is, the fluid escaping from the ulcerated surface, but being pent up in the comparatively healthy tissues around. In the history of almost all ulcers there comes a period at which healing takes place, the sloughs gradually separating and leaving a clean red surface covered with a very fine transparent film; sometimes this film becomes slightly opaque and greyish, and from it comes away, constantly, a fluid (pus) often very readily removed, leaving the surface perfectly clean. Examining such an ulcer where the healing process has begun, it will be found that the loss of tissue has in some way been compensated for, the fleshy granulating surface now coming up to the level of the margins of the wound; if this granulating surface be roughly handled or pricked, it bleeds readily, being exceedingly vascular, especially towards the centre; nearer the margins it is usually somewhat paler. At the extreme margin a delicate pellicle may be seen, at first red, then slightly bluer than the granulation tissue, further out purple, then blue, and gradually shading off from this into the white of the surrounding normal cutaneous tissue; this is known as the "healing margin," the opacity being due to the growth inwards of the epithelial cells, which gradually cover the granulation tissue. Remove the margin of such an ulcer. Harden (§ 58, 59, 61, or 63). Cut (§ 82 *et seq.*). Stain and mount (§§ 103 or 110 (*b*), 132, 162, and 199).

($\times 50$).—Near the middle of the surface of the ulcer there is a thin layer of disintegrating cells, some of which are swollen and hyaline, others granular, but all of them imperfectly stained; they take on a brown coloration with picro-carmin, or red with logwood and eosin. Between these cells lies coagulated fibrinous lymph, usually in

very small quantities. Beneath this layer, which corresponds to the greyish layer of pus, there may be seen, though not where healing is going on rapidly, small scattered spaces filled with blood; these are partly lined by flattened endothelial cells, and appear to be dilated embryonic capillary vessels, which, unprotected by tissues near the surface, become over-distended, small hæmorrhages resulting either at or near the surface. Immediately below this fibrinous and cellular layer comes a course of vessels running more or less transversely; these are evidently the convex arches of loops of capillaries, as from them double rows of spindle-shaped cells may be traced downwards, first in an oblique direction, and then at right angles to the surface. Both above and below these loops are numerous spindle and round cells; the smaller round cells, which are found in little groups, are evidently leucocytes which have escaped from the dilated vessels, in the immediate neighbourhood of which they are always found. The spindle cells and larger round mononucleated hyaline cells, each with a distinct rounded or oval nucleus and a well-marked protoplasmic body, are found between the vascular loops. Near the surface the spindles, fibroblasts, run parallel to the axis of the blood vessels, both in the curved and in the straight parts of the loops, but in the deeper layers of granulation tissue many of the spindle cells run at right angles to the axis of the vessels, giving rise to a peculiar basket-work appearance, the bundles of cells appearing to interlace backwards and forwards, behind and in front of the new vessels. At one or two points are seen large plasmodial cells, some of them with several nuclei, almost like bone osteoclasts, but not quite so large nor with so many nuclei; these appear to correspond to Ziegler's fibroplastic cells or fibroblasts; large single nucleated cells are also present in enormous numbers wherever the organisation is at all advanced, in fact, wherever the new blood vessels have penetrated. Here, also, the large plasma cells, with their small deeply-stained points, are very numerous. These may be seen distinctly even under the low power.

On tracing the course of the new blood vessels it will be found that they all come from the deeper layer of healthy tissue, and wherever buds are leaving these tissues there is usually an accumulation of leucocytes around sinuses of considerable size, from which the new blood vessels are given off, though, in some cases, they appear to arise directly from the older vessels without any previous formation of sinuses.

II

III

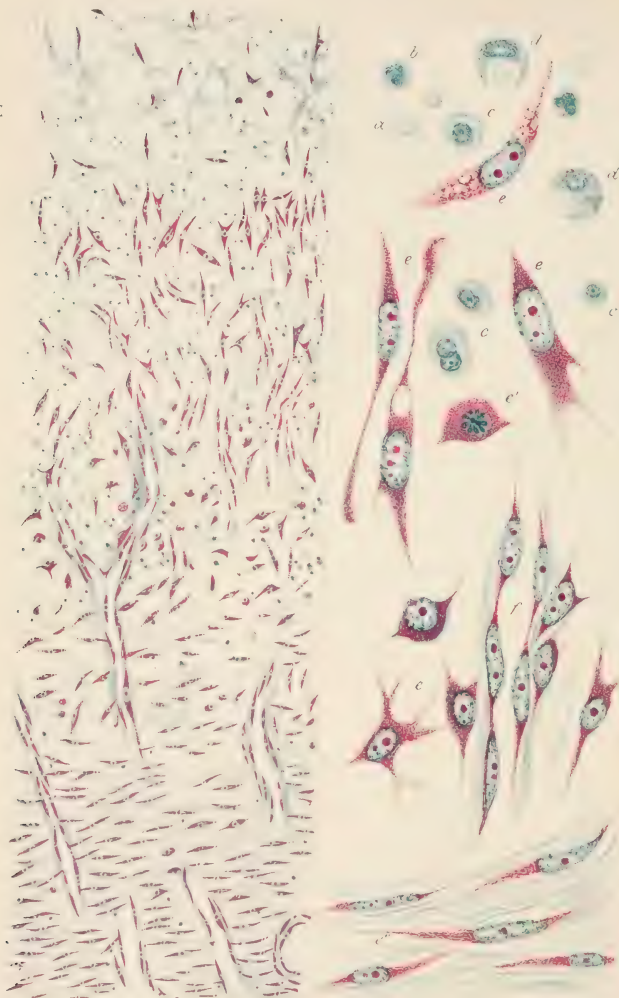


FIG. 20.

Passing to the margin of the ulcer where the epithelium is creeping in, it will be seen that the blood vessels, although not nearly so prominent, nor so regularly arranged, can still be seen passing up, almost to the under surface of the epithelium. The connective tissue cells are more regularly arranged; most of the polymorpho-nuclear leucocytes have disappeared, and only a few hyaline mononucleated cells, some lymphocytes and more numerous spindle and branching cells (fibroblasts) remain; these usually form a delicate, almost myxomatous-looking cellular tissue. Sometimes, however, in the deeper layers, a large number of leucocytes can still be seen surrounding the vessels that remain, and it is only as we pass away from the ulcer that the number of nuclei becomes diminished, the blood vessels become better developed, and the tissue becomes more truly "connective" in type. At a distance from the wound, note the usual pink fibrous tissue basis with a small number of spindle cells with elongated nuclei lying between or on the bundles of pink fibres.

Coming now to the epithelium, note that it creeps inwards by lateral extension from the margins of the ulcer, evidently growing from pre-existing epithelium; at first it undergoes very rapid degenerative change, and there is seen, on an irregular layer of squamous epithelium, a distinct yellow horny layer. This ingrowth at the margin follows the irregularities of the granulating surface, and, should there be any marked pit or depression, the epithelium grows down into it, sometimes for a considerable distance, giving rise to the

Description of Fig. 20.

FIG. 20. Granulating surface of a seven days' ulcer. Stained by Unna's modification of Pappenheim's pyronin methyl-green stain as used by Maximow. ($\times 150$.)

- I. Superficial layer, composed mainly of fibrin.
- II. Intermediate granulation tissue, cellular layer becoming vascularised.
- III. Layer of old fibrous tissue.
 - a. Red blood corpuscles.
 - b. Polymorpho-nuclear leucocytes.
 - c. Mononucleated cells, large and small. Macrophage and lymphocyte.
 - d. Mononucleated cells, phagocytic.
 - e. Fibroblasts.
 - e'. Fibroblasts, undergoing mitotic division.
 - e''. Spindle-shaped fibroblasts.
 - f. Young capillary vessel.

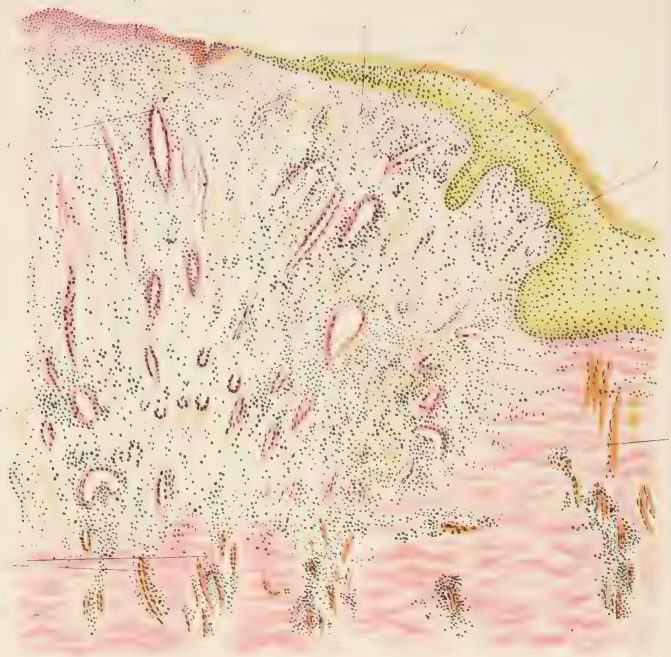


FIG. 21.—Section from a healing ulcer of the leg. Stained with alum hæmatein and van Gieson's stain. ($\times 20$.)

- a.* Layer of fibrinous lymph and pus cells, mostly altered polymorpho-nuclear leucocytes lying on the granulating surface.
- b.* Invading margin of epithelium.
- c.* Epithelial layer with well-formed papillæ, due to dipping down of processes into spaces between loops of vessels.
- d.* Connective tissue cells and active leucocytes near the surface and around the sections of transverse portions of vascular loops (*e*).
- f.* Vertical or limb parts of vascular loops passing to the surface.
- g.* Groups of leucocytes around the young blood vessels.
- h.* Older, more perfectly formed vessels shooting from the deeper tissues.
- i.* Corium proper, composed of hard fibrous tissue.
- j.* More cellular new tissue in which vessels still remain, although the new tissue is now covered in by a well-formed epithelial layer.

formation of a kind of epithelial barrier which, in some instances,



FIG. 22.—Granulating ulcer stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Fibrinous coagulated lymph at the surface of the wound.
- b.* Small round cell, probably a polymorpho-nuclear leucocyte.
- c.* Spindle-shaped connective tissue cell.
- d.* Vascular loop, transverse part.
- e.* Vertical limb of same. Evidently formed by double rows of elongated cells.
- f.* Polymorpho-nuclear leucocytes, lymphocytes, and rounded connective tissue cells.
- g.* Spindle-shaped connective tissue cells, fibroblasts.
- h.* Transverse spindle-shaped cells (with basket-work arrangement) which ultimately form firm fibrous tissue and cause constriction of many of the new vessels.

interferes very materially with the healing of the wound. (Hamilton

gives this as one of the chief causes of the slow healing of ulcers.)

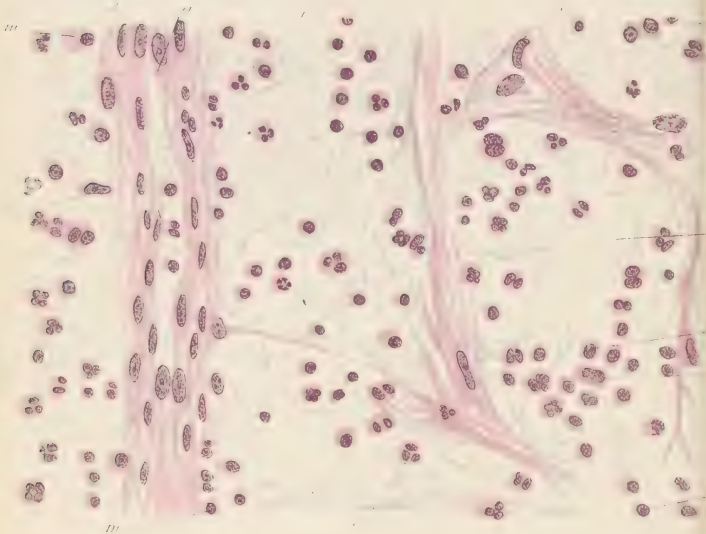


FIG. 23.—Section from healing ulcer of leg. Stained with logwood and eosin. ($\times 600$.)

- a.* Wall of fairly well-developed blood vessel, in which are both red and white blood corpuscles.
- b.* Connective tissue cell with nucleus, outside the vessel (in the tunica adventitia).
- c.* Free, rapidly dividing connective tissue cells.
- d.* Nuclei of endothelial cells lining a vessel.
- e.* Nucleus and protoplasm of fixed connective tissue cell (fibroblast) lying on a bundle of fibrous tissue.
- f.* Large cell in which the nucleus is undergoing mitotic or karyokinetic division.
- g.* Spaces filled with cedematous fluid separating fibrils, and allowing the cells to be seen more distinctly.
It is probable that the imperfectly stained and irregular bodies in some of the cells are really partially digested leucocytes or other material taken up by the "macrophages."
- h.* Mononuclear, hyaline cells, macrophages.
- i.* Polymorpho-nuclear leucocytes.
- k.* Mast cell.
- l.* Lymphocytes.
- m.* Plasma cell.

In consequence of these irregularities the thickness of the layer of

epithelium, even at the healing margin, varies considerably at different points, but it may be observed that it does not vary more than, in fact not so much as, on ordinary cutaneous surfaces; it is owing to these irregularities that new papillæ are seen when the healing process is completed.

($\times 300$).—All the above points may be made out more readily. Special attention should be paid to the following:—The degenerating surface where numerous polymorpho-nuclear and mononucleated cells and fragments of fibrin may be easily distinguished. At the lower part of this layer are a few fibroblasts. Below this is a layer of tissue in which the new blood vessels, derived from the endothelium of the blood vessels of the deeper layers, may be seen. Between these blood vessels the delicate connective, almost myxomatous, tissue is made up of spindle-shaped or irregularly branched cells, fibroblasts, and large and small rounded mononucleated cells, with here and there a few polymorpho-nuclear leucocytes lying on the strands or in the meshes of the network.

Some of these fibroblasts or fibroplastic cells are of considerable size. A number of plasma cells and, here and there, even mast cells may be observed, especially in the perivascular lymph spaces; also the blood corpuscles lying between the parallel lines of flattened endothelial cells which constitute the blood vessels of the granulation tissue.

In the fibroblasts mitotic division of the nucleus can often be made out, whilst, here and there, large well-formed fibroplastic cells lying on bundles of fibrous tissue may be seen just at the margin of, or in the deeper layers of tissue beneath, the ulcer. This is especially the case where the tissues are oedematous, *i.e.* where there is an accumulation of fluid in the spaces of the connective tissue network. The elements of fibrous tissue and the various forms of nucleated cells may be seen very distinctly (see Fig. 23, which is taken from the margin of a somewhat oedematous very slowly healing ulcer). The healing process in an ulcer is very similar to that met with in other positions to which reference has already been made. The development of the cicatricial tissue may be readily followed; the connective tissue cells or fibroblasts gradually give place to fibrous tissue, a large part of the protoplasm of the cell being "replaced" by a fibrillated matrix, whether by secretion or by direct differentiation of the protoplasm it is difficult to say. The old spindle-shaped fibroblasts

and the dilated original vessels may be seen, very distinctly, below this open myxomatous-looking layer of the newer reparative tissue.

"VEGETATIONS"

226. In acute endocarditis or aortitis the structure of fibrinous vegetations may be studied very readily. The appearances presented are very similar to those seen where there is exudation of fibrinous lymph and organisation in the coagulated exudate on a pleural or pericardial surface. Vegetations, which usually occur along the lines of contact of the valves, or where there is irritation by friction of the wall of the aorta, may appear as small or larger semi-transparent, or opaque greyish or greyish-yellow wart-like bodies, projecting for some little distance into the blood stream; they may be easily detached with the finger-nail; they crumble down readily, and on section are somewhat laminated, and at points blood-stained. When separated from their base they leave a roughened slightly projecting surface. Harden a valve or piece of the aorta with attached vegetation (§ 58). Stain (§ 102, 103, or 104), clear (§ 193), and mount (§ 199).

($\times 50$).—The fibrinous lymph, as it is deposited, usually on a roughened endocardial surface, is directly in contact with the blood stream; consequently an enormous number of leucocytes, many of them more or less broken down, are deposited not only on the surface, but also in the spaces between the layers of fibrin which have from time to time been deposited from the blood. Deeper down, where the fibrin is not in contact with the blood stream, and where corpuscles have not been carried from the tissues below, the leucocytes have disappeared (broken down to supply fibrin ferment) and the granular coagulated lymph is in all respects like that met with on other serous surfaces, where the leucocytes have disappeared during the process of fibrin formation. We have simply a network of strands of coagulated fibrin. There is lamination even in a small clot such as this, *i.e.* we have a layer of fibrin in which there are no corpuscles (probably made up in a great part of blood "*plaques*," with a few leucocytes), then a layer in which the fibrin has in its meshes a large number of leucocytes and red blood corpuscles, and so on in alternate layers. This, of course, depends on the size of the clot. The lamination is of much the same nature as that met with in the clot in an aneurism,

which is usually laid down in very regular, successive, layers. Below the clot there may often be seen a layer of granulation tissue to which



FIG. 24.—Vegetation on the wall of the aorta from a case of acute aortitis. Stained with alum hæmatein and picro-erythrosin. ($\times 20$.)

- a. Vegetation, fairly smooth on its surface, composed of a reticulum of fibrin, in the meshes of which are numerous leucocytes.
- b. Indications of lamination near the surface.
- c. Central part of vegetation in which the fibrin contains very few leucocytes. See also *d* near blood stream.
- e. Swollen laminated intima with numerous proliferating cells.
- f. Prominent vasa vasorum in muscular layer leading from
- g. Similar vessels in connective tissue and elastic layer.
- h. Masses of polymorpho-nuclear leucocytes surrounding these dilated vessels.

it is firmly adherent, and small blood vessels appear to be making their way from the granulation tissue into the fibrinous mass. Embedded

in this granulation tissue are small masses of fibrin which are evidently being absorbed by the advancing granulations. Below this, strands of muscle fibre and a large amount of connective tissue, in which some of the blood vessels are enormously dilated and surrounded by numerous round cells, are seen; there are also a number of blood vessels around which more irregular (connective tissue) cells are developed in considerable numbers; the vessels in this layer are tortuous. Between the elastic laminae the amount of new tissue is very considerable; it is made up, principally, of large fixed connective tissue cells, with well-marked nuclei, a few leucocytes being distinguished here and there, especially in the immediate neighbourhood of the blood vessels. These round cells usually occur in small groups, and are especially well marked at those points where the granulation tissue appears to be growing at the expense of the muscular and elastic fibres.

In this specimen note the appearance of the surface of the fibrin; owing to the pressure and friction of the blood stream flowing over it, it has acquired a smooth, slightly compressed surface; note the reticulum of fibrin (red with eosin) with the large number of leucocytes (small deep blue points) embedded in it; in the centre of the mass the fibrinous reticulum contains few leucocytes. This fibrinous vegetation rests on a layer of tissue in which a few small loops of embryonic blood vessels, some of which appear to be projected directly from the dilated vessels immediately below, others to be of entirely new formation, may be seen. This, however, is not a very marked feature. The vessels from which the loops are projected may be distended, and are frequently surrounded by small masses of leucocytes and lymphocytes into which the loops appear to project. The cells in the deeper layer of the intima or endocardium have at this stage developed a quantity of protoplasm around their nuclei, so that here the intervals between the nuclei appear to be greater than near the surface. The vessels in the muscular coat and even in the adventitia appear, in this case, to be distended and surrounded by polymorpho-nuclear leucocytes.

Here, then, are all the conditions present on an inflamed serous membrane on which organisation is taking place, the only marked difference being that a great part of the fibrinous clot is deposited, not from the small distended vessels coming to the inflamed surface, but from the blood passing over it; consequently the organisation of this clot is not nearly so far advanced as it is on a pleural surface where the changes in the deeper tissues are always much more marked than they

are in this position. It must be remembered that organisation invariably takes place from subjacent tissues, and that channelling or tunnelling of a clot is not true organisation. The fact that the leucocytes and lymphocytes in the lumen of the vessel cannot give rise to organising connective tissue cells near the surface of the clot, where there can be no question of want of nutrition, is a very strong argument against the formation of any connective tissue from these circulating cells. On the other hand, where we have the young connective tissue cells (hyaline and plasma cells) in large numbers in the deeper layers, into which they can be carried or make their way very readily along with advancing blood vascular loops, the formation of new connective tissues invariably goes on rapidly.

($\times 300$).—All the above features are now more distinctly seen. In the wall of the aorta the laminae are swollen and separated by groups of cells, there is considerable dilatation of the vessels of supply; numerous branches—many of them little more than embryonic capillaries—to be seen running in the altered coat, are given off from the larger vessels. At the junction of these small vessels with the larger branches, from which they spring, leucocytes, lymphocytes, plasma cells, large mononucleated cells, and fibroblasts (young connective tissue cells) accumulate in large numbers; but it will be noted that as the surface on which the fibrin is thrown out is approached, more leucocytes are present, large mononuclear cells, fibroblasts, and endothelial cells, though still numerous, are not nearly so well developed as in the deeper layers. The vessels, few in number, that are pushing their way into the fibrin have a very rudimentary structure, they consist simply of flattened, endothelial cells arranged in double rows, with blood corpuscles lying between them. Around each of these vessels, rudimentary as they are, is a space sometimes bounded only by compressed fibrin, with a cell nucleus here and there, but very frequently by a layer of flattened cells, so that even at this early stage a kind of perivascular lymph space (see Fig. 29 II.) is formed, in which leucocytes, plasma cells, and large mononuclear cells are sometimes present in considerable numbers. At certain points the vessels are passing singly into the fibrinous scaffolding, but at others whole groups of vascular loops project into it, carrying with them a quantity of comparatively well-formed connective tissue. From these little bundles of loops small budding vessels, which are quite distinct in structure and appearance from the larger projected vessel, may be formed. Although

all these points may be made out, it will be noted that the formation of the blood vessels is by no means such a constant or prominent feature as it is on most inflamed serous surfaces. Where these vessels are shooting upwards, the number of leucocytes in the fibrin is exceedingly small, this latter forming a network of delicate threads. Still nearer the free surface the leucocytes, derived from the blood stream, and deposited in layers on the surface of the vegetation, are very irregular in shape, and are usually much broken down, though they still may take on a distinct logwood stain. Amongst the larger cells, many of which appear to be undergoing irregular division, are numerous very minute corpuscles, often deeply stained, which may be the result of the disintegration of the leucocytes, though some of them are possibly blood plates; here and there altered red blood corpuscles or little specks of pigment may be seen in large numbers. At no point near the clot is there any trace of lining endothelium left, but at the margin there is marked increase of the intima with extreme vascularisation, even where the vessel wall is not actually covered by the coagulum; the proliferating hyaline large mononuclear cells, fibroplastic cells, and distended blood vessels in the inflamed and thickened intima are distinctly visible.

RELATION OF INFLAMMATION TO REPAIR

227. It will be gathered from the description given of healing and later of abscess formation, that in these conditions, and even in injury to the tissues, inflammation plays a very prominent part, that it is, in fact, in most cases an essential factor in localising necrosis and in the production of new tissue for the repair of any breach of continuity or loss. At the same time it must be borne in mind that all inflammation is dependent upon irritation, and that any one of its features can be looked upon only as part of a complex process, and that in those cases where there is an actual breach of continuity the amount of inflammation may be very slight if the loss of tissue is small, or if the bruising is slight and the parts be again brought into very close apposition. Healing by direct union is then associated with but little evidence of inflammation either in the form of pain, swelling, heat, or redness. Where, however, tissues are bruised, or where the gap to be filled up is of considerable size, then inflammation ensues, the severity and extent of which are entirely determined by—(1) the amount of direct damage done to the tissues and of the irritation to which they are in

the first instance subjected ; (2) the subsequent irritation by organisms, chemical irritants, pressure, chafing, etc. ; and (3) the amount of dead material or temporary scaffolding that has eventually to be removed.

Looked upon in this light, inflammation, though theoretically necessary only in a minor degree, is practically associated with most of those conditions that come under the observation of the pathologist. This is brought into still stronger relief when it is remembered that inflammation must be looked upon as comprising all those reactionary phenomena that are manifested by the various tissues when they are subjected to long-continued or very powerful abnormal stimulation.

Inflammation is not associated merely with the changes that take place in the walls of the blood vessels, or with those that occur in the lymphatic and connective tissue systems that surround the vessels, or with those only that may be observed in cells lining large endothelial sacs, the cells that cover the omentum, the parenchymatous cells of the various organs, the cells lining the alveoli or the bronchial tubes of the lung, or, in fact, with any single set of tissues ; although it is a manifestation of the reactions of the tissues as a whole to increased noxious stimulus, it is not dependent upon any one of these sets of tissues for its full development. Inflammatory changes may occur in a tissue entirely devoid of ordinary blood vessels just as certainly as it may occur in tissues in which we can find no epithelial cells, but if these structures are present in any tissue subjected to irritation, they will apparently, as a matter of course, take part in the general inflammatory process.

For the inflammatory changes in different organs we refer to the sections in which special diseases are described ; but it may be well here to recapitulate certain facts connected with inflammation, abscess formation, and repair.

In the first place, cells that, under ordinary conditions, proliferate, do so much more rapidly under special stimulation : such proliferated cells, when the division is going on rapidly are, at first, embryonic in form, and are endowed with the general characters of primitive protoplasm : usually they are more motile than normal cells, more plastic, and appear to exhibit a greater power of ingesting foreign bodies ; under continued abnormal stimulation these characters are retained and even accentuated, but when the stimulation is gradually diminished the embryonic cells may revert to their original adult form, and give rise to the formation of tissue similar to that which, under normal conditions, they were

engaged in building up. The more highly cells are specialised the less readily do they lose their form and functions under stimulation without being entirely destroyed, but the less readily do they revert to their original form when the stimulus is removed. It is found, as a matter of fact, that if irritation be long continued, these higher cells are apt to be superseded by those of lower, *e.g.* connective tissue, types. If this be borne in mind it will be an easy matter to understand how it is that various fibroid changes are met with in organs in which, normally, most of the cells have a specialised function, and the amount of connective tissue is comparatively small. Then, again, degenerated specialised cells always appear to act as foreign bodies, and until they or their débris are removed there can be no return to health; even some of those which retain a certain amount of vitality being unable to return to the normal or to carry on their function in any satisfactory fashion.

SUPPURATION

228. Under the action of any powerful irritant, a certain number of cells are usually so stimulated that their protoplasm is never again able to return to its normal condition, they die (poisoned or over-stimulated) and must be removed to make way for others. How this takes place can best be seen in abscess formation.

ACUTE METASTATIC MILIARY ABSCESS OF THE HEART IN ULCERATIVE ENDOCARDITIS

229. In certain cases of ulcerative endocarditis small yellow points, sometimes almost microscopical in size, but more frequently the size of a millet seed, are seen in the muscular wall of the heart. These are specially numerous, or, to be more accurate, are specially well seen near the endocardial surface. Such yellow points are also met with in other organs and in the subcutaneous connective tissue, and appear to be formed around septic emboli which, derived from the breaking down vegetations in ulcerative endocarditis and composed of a network of degenerating fibrin in which are entangled cells and micrococci, become fixed in the small terminal or capillary vessels of the various organs. These abscesses are usually multiple, and they follow, most closely, the distribution of the blood vessels. If they can be examined at a sufficiently early stage, the appearances presented are extremely

characteristic. Each has a small yellow or yellowish-grey centre ; then comes a grey, sometimes translucent, zone which, before shading off into the normal tissue, is often surrounded by a delicate red or reddish-purple zone. In some cases, where the breaking down of the tissues is going on rapidly, this hyperæmic zone is so ill defined that it can scarcely be distinguished. In the immediate neighbourhood of the minute abscesses, or even in their substance, small hæmorrhages are often found. Harden (§ 61, 62, or 63) a small piece of the muscle from the wall of the left ventricle, care being taken to note that it contains one of the small abscesses ; stain the sections by Gram's method (§ 173), using a contrast stain, clear (§ 193), and mount (§ 199).

($\times 50$).—The abscess can be recognised at once. In its centre is an oblique section of a vessel, evidently plugged with a mass of micrococci, which stands out very prominently. The wall of the vessel and the small amount of remaining surrounding tissue are both somewhat homogeneous in appearance ; immediately outside this are numerous polymorpho-nuclear leucocytes and lymphocytes, with here and there a few larger cells, which are to be looked upon as proliferating fixed connective tissue (hyaline) or fibroplastic cells.

At the margins of the abscess the transition from abscess to muscular tissue is very abrupt, the leucocytes along with the digestive enzymes of the micrococci apparently causing rapid disintegration of the muscular fibre. At one or two points a slight increase in the number of nuclei between the muscle fibres may be observed. Near the inner part of the wall of the heart, the proliferation of the endocardial cells is well marked, this proliferation gradually tailing off on each side of the "pointing" abscess, so that over the abscess is a thickened cellular layer. This closely resembles the condition met with in endarteritis. The ends of the muscle fibres abutting on the abscess are somewhat irregular, and are evidently being absorbed. In the immediate neighbourhood of the abscess, and in what is evidently part of the plugged vessel, there is an increase in the number of leucocytes within the lumen of the vessel. These leucocytes appear to have collected at this point in large numbers, partly as the result of chemiotactic action, and partly in consequence of the obstruction to the blood-flow immediately beyond.

($\times 300$).—The structure of the abscess is now more evident ; the mass filling the lumen of the vessel is seen to be made up of small cocci ; immediately around this mass the wall of the vessel and portions of the

muscle are quite homogeneous and are very imperfectly stained. In the unstained area, seen under the low power, are numerous nuclei, appar-

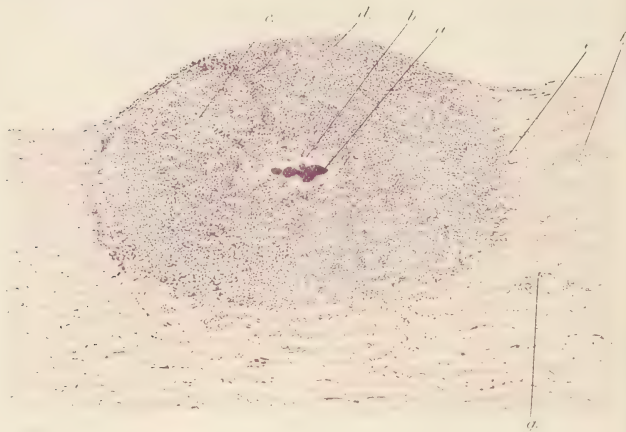


FIG. 25.—Acute metastatic miliary abscess immediately under the endocardium, from a case of ulcerative endocarditis; stained by Gram's method, but only partially decolorised; contrast stain—eosin. ($\times 50$.)

- a.* Mass of micrococci (which may be partly of post-mortem growth) impacted in a small blood vessel.
- b.* Altered, partly "digested," wall of the blood vessel, with a similar change in some of the surrounding tissue. This tissue is imperfectly stained, and is almost homogeneous.
- c.* Mass of leucocytes and proliferated fixed connective tissue cells, forming a kind of barrier between the dead and the normal tissues; here and there fragments of unstained muscle may be seen.
- d.* Proliferating cellular layer of the endocardium. A mass of flattened cells.
- e.* Margin of abscess, near which the larger connective tissue mononuclear (hyaline) cells, fibroplastic cells, and plasma cells are always most numerous. The line of demarcation is very distinct.
- f.* Small vessel in which are numerous leucocytes.
- g.* Small vessel seen in transverse section. A small collection of polymorpho-nuclear leucocytes and lymphocytes is seen in the perivascular lymph space.

ently those of dead or degenerated polymorpho-nuclear leucocytes and of large and small mononuclear cells, which do not take on the stain

nearly so deeply as do those in the surrounding tissues. Between these nuclei are granular fragments of muscle fibre which have lost much of their ordinary or typical structure and appearance. Outside this area comes a zone of leucocytes deeply stained, evidently very active, with here and there a larger mononucleated hyaline cell, or a cell with one or two deeply stained nuclei, derived, apparently, from the fixed connective tissue cells (fibroblasts). At the extreme margin of the abscess these fixed connective tissue cells are more numerous ;

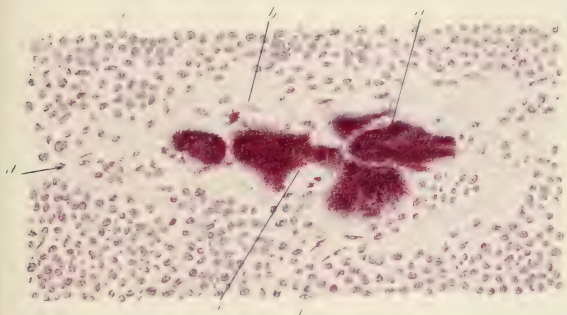


FIG. 26.—Acute miliary abscess immediately under the endocardium, from a case of ulcerative endocarditis, stained by Gram's method, but only partially decolorised ; contrast stain—eosin. ($\times 420$.)

- a.* Plugs of micrococci. These have made their way into or even through the wall of the vessel.
- b.* Altered (digested?) vessel wall.
- c.* Leucocytes, many of them breaking down, thrown out in large numbers immediately around the vessel.
- d.* Altered (digested?) muscle fibre around vessel.
- e.* Digested leucocytes and lymphocytes, very imperfectly stained, in the immediate neighbourhood of the micro-organisms, some of them are seen to contain large numbers of these micrococci.
- f.* Larger and more elongated connective tissue cells.

the muscle fibres look like "ghosts" of fibres, fragments of the sheath remaining, with, here and there only, fragments of much degenerated, vacuolated, or granular muscular fibre. Between these fragments, and even between the healthier muscle fibres, polymorpho-nuclear leucocytes and lymphocytes are making their way in considerable numbers. The thickening of the endocardial layer with the proliferation of the cells forming it is well marked, especially at the margin of the abscess (not shown in Figs. 25 or 26). These cells are arranged in flattened, com-

paratively regular layers, immediately on the endocardial surface ; they may be traced over the round-celled mass, of which the main part of the abscess is composed. The distended vessel in the immediate neighbourhood of the abscess contains a number of polymorpho-nuclear leucocytes, and a considerable number of cells with proliferating nuclei, each surrounded by a large body of cytoplasm. The endothelial cells lining the vessel are evidently proliferating, and it appears probable that some, at least, of the larger cells are derived from this endothelial lining.

In this specimen we have an exceedingly good illustration of the process of abscess formation. A micrococcus (§ 229*a*) has made its way with an embolic mass to the minute vessels in the wall of the heart ; this embolus becomes impacted in vessels supplying tissues that are already altered by malnutrition ; in a medium now at rest, the fibrinous clot, in which the products of these organisms have accumulated, the micrococcus is enabled to proliferate and so give rise to a large mass of organisms (this proliferation may have been continued after the death of the patient). As in all cases of inflammation the blood vessels in the surrounding area, especially the minute venules and capillaries, have become dilated ; there has been slowing of the blood current, with emigration of leucocytes ; this is accompanied, or soon followed, by a bringing up of lymphocytes. The products of the micro-organisms acting on the tissues in their immediate neighbourhood have set up a kind of digestion of the muscle fibres and other tissues, and the nuclei now degenerating take on stains very imperfectly or not at all. Following or accompanying all this, there has been a further migration of leucocytes from the distended vessels into the degenerating area, these leucocytes gradually making their way to the centre of the abscess, and removing the degenerated products. In this process a number of the "phagocytes" are destroyed and disintegrated by the peptonising products of the micro-organisms, and at the stage at which this abscess is examined there appears to be an area immediately around the proliferating organisms, outside which the leucocytes are kept at bay (negative chemiotaxis) by the micro-organisms or their products. As the abscess increases in size, more and more of the leucocytes near the centre become digested, but in the immediate neighbourhood a series of reinforcing leucocytes form a barrier to the advance of the bacteria, either temporary or more permanent in character, according to the vitality of the tissues on the one hand, and

the activity of the micro-organisms on the other. As a rule, these micro-organisms cannot obtain a foothold in the circulating blood or tissues of healthy individuals, but wherever there is malnutrition, or lowered vitality of the tissues through injury or previous inflammation, the organisms are able to take up a coign of vantage from which to attack surrounding tissues, though, even in the case of acute abscesses, localisation usually takes place sooner or later.

Although polymorpho-nuclear leucocytes are here specially described, it will be found that numerous pseudo-lymphocytes (polymorpho-nuclear leucocytes, in which, owing to degenerative changes the nuclei have assumed a more or less rounded and condensed form) and true lymphocytes with a few plasma cells and large mononucleated hyaline cells soon make their appearance in this position. The latter type of cell is actively phagocytic, for in its substance not only cocci are found but partially digested red blood corpuscles and polymorpho-nuclear cells containing, in turn, imperfectly stained cocci. Evidence of proliferation of the fibroblasts and of the endothelial cells should also be noted.

It is stated that bacteria usually gain access to the tissues by way of the blood vessels, and in very acute cases this is undoubtedly the case, but it is now proved that in many cases these micro-organisms spread, though of course not so rapidly, by the perivascular and other lymph channels. This is a most important point to note in connection with the proliferation of cells to be seen in these positions.

From this we gather that when a plug containing pyogenic micro-organisms becomes impacted in a small vessel, or when micro-organisms find their way from without into tissues that have their vitality impaired, these organisms acting on the proteids of the tissues, and in process of their own development, give rise to the formation of a poisonous chemical substance which, acting as an irritant, or by its direct digestive action on the protoplasm, brings about a process of degeneration which has been compared to that induced by the enzymes when acting on albuminoid materials; in the immediate neighbourhood of these organisms both highly organised cells and connective tissues are, in fact, digested. This digested material at once commences to act as a foreign body and as a chemiotactic agent; it will be found that around and gradually invading it are numerous small round nucleated cells, the majority of which appear to have come from the blood vessels. Most of these, as Cohnheim pointed out, are probably polymorpho-nuclear leucocytes, especially when the process goes on rapidly,

but there are also seen a number of lymphocytes which may have come up by way of the lymph vessels, or which, like the larger mononuclear cells and fibroblasts, may be derived from the fixed connective tissue cells, or from the endothelial cells that line the lymph spaces around the vessel. These cells, the result or manifestation in this position of the presence of inflammatory processes—emigration and proliferation—play a most important part, both in localising the area of activity of the products of micro-organisms and in removing dead or effete matter. They may be thrown out as soon as the irritation commences, but where the number of micro-organisms is large, and where they are able to form a considerable quantity of their special ferment or irritant matter, the cells may be killed before they have time to proliferate, and migration may be prevented—*i.e.* we have a condition of negative chemiotaxis. When, however, the cells are thrown out, although attacking both the organisms and their products, a number usually succumb and go to swell the quantity of dead material; this may go on time after time until a large mass of dead cells has accumulated in the neighbourhood of the septic embolus. Sometimes the process of breaking down of the tissues and cells is so perfect, and the quantity of fluid escaping with these cells is so large, that a considerable area of tissue may become resolved into “pus,” which is made up of many dead leucocytes, of a few living ones, of a quantity of fluid derived from the distended blood and lymph vessels, of digested “fixed” tissues, and of micro-organisms, usually in various stages of degeneration.

Whether the quantity of digested tissue (in which the presence of peptones may actually be demonstrated) be large or small, there is usually a zone outside the mass of pus in which the polymorpho-nuclear leucocytes take on the usual staining reactions, and are therefore nearer a normal condition. If these marginal cells be examined, it will be found that they frequently contain very minute vacuoles, and that embedded in their substance are more or less perfectly stained micro-organisms, *i.e.* micro-organisms in various stages of degeneration. Metchnikoff observing this, has concluded that these cells act as “phagocytes” or devourers of dead tissues and noxious organisms. There can be little doubt that these cells do take up micro-organisms, but whether before or after the micro-organism is dead is an exceedingly difficult point to settle, for it must be remembered that micro-organisms may be very distinctly stained, even after they are dead, if degeneration

has not commenced ; it must also be borne in mind that what micro-organisms can do animal cells can also effect, and that these leucocytes throwing out a digestive fluid, or at any rate some material detrimental to the existence of micro-organisms, may prepare the organisms, killing and even partially digesting them, then taking them into their protoplasm as inert matter, and there continuing the process of digestion.

It will be remembered, however, that in addition to the small polymorpho-nuclear neutrophile cells above described, larger hyaline cells are found, such cells usually being numerous where the process is already localised, to a certain extent, by the leucocytes, so that in the outer part of the wall of an abscess they may usually be very distinctly made out. At this stage they appear to have much the same function as the smaller cells, and one can often see within the protoplasm of these large nucleated cells, small spaces enclosing granular, imperfectly stained leucocytes, red blood corpuscles, or, it may be, particles of pigment derived from red corpuscles, in fact, any dead or partially degenerated material with which they may come in contact. These, as above noted, are always more numerous where the process of localisation is complete, and it would appear that they take up and carry on slowly the work of digestion of foreign tissues which the polymorpho-nuclear leucocytes or microphages of Metchnikoff have commenced ; and, comparing the process to a battle between organisms and the cells, a simile that is often used, the leucocytes may be described as the light cavalry which can be rapidly brought up and massed at any one point to deal with invading organisms, especially those of bacterial type ; whilst the larger cells, macrophages, derived from the fixed connective and endothelial tissue, may be looked upon as the heavy infantry which completes the work, taking up both bacterial and animal parasites, and other animal cells, red blood corpuscles, leucocytes, lymphocytes, etc., and afterwards repairs the damage that has been done by the invading army. All the changes met with in inflammation are associated with the bringing up of these cells to the point at which injury occurs ; all the processes of healing are connected with the necessity of making good in as perfect a manner as possible the damage that has been done ; the two processes, therefore, cannot usually be dissociated. The processes of inflammation clear the ground of dead or effete material, and lay the foundation, or rather form the scaffolding, on which the processes of repair are afterwards carried out.

On incising a swelling which we know from experience would

ultimately become converted into an abscess, it is found that although in some cases there is great accumulation of fluid in the lymph spaces, the tissues are firm and hard; from these hard tissues there slowly exudes a quantity of comparatively clear fluid. In the swollen mass there may be a small central point, yellow and opaque, but not yet distinctly softened; whilst throughout the section, on examination with a hand lens, smaller opaque points may be seen, with, here and there, a number of glistening areas. A considerable amount of blood escapes from the cut surface, this indicating engorgement of the dilated vessels. If the swelling be examined at a sufficiently early stage, it may be determined by microscopic examination that the lymph spaces are enormously distended with coagulated fibrin, with lymphocytes, leucocytes, and proliferating cells, apparently derived from the endothelium lining the spaces (these latter are not very numerous); embedded in the fibrin are many micrococci, usually arranged in definite chains, or in little heaps. It is an exceedingly difficult matter to obtain sections of abscesses at this stage, but this condition is here described in order that the process of suppuration may be followed and understood in its later stages, especially in those cases in which the irritant organisms have made their way to the part by means of the lymphatics.

Pus

229*a*. If the pus from an acute abscess be stained (§ 173) and examined ($\times 450$) immediately after it is evacuated, the pus corpuscles (some of them still distinctively stained, others undergoing fatty and granular degeneration) may be readily distinguished. Most of these corpuscles are polymorpho-nuclear leucocytes (microphages), though here and there a few lymphocytes and larger mononucleated cells (macrophages) may be found. Between the cells, and in some few instances actually within them, various forms of micro-organisms, usually staphylococci or streptococci, may be found. In the early stages of pus formation these micro-organisms are almost invariably demonstrable, but in the later stages, when the abscess is opened, it is often difficult to find a single coccus even where the suppuration is very extensive.

Some of the pus corpuscles, during the very early stages (or when taken from an inflamed mucous surface), when examined on a Stricker's warm stage, or in a warm chamber, still exhibit amœboid movement; they send out little processes, retract them, undergo change of shape,

and generally behave much as do normal cells under similar conditions, though, usually, they are not quite so active. In the later stages of suppuration most of the cells have lost their amœboid movement, they are fatty and granular, the granularity becoming more and more distinct as the cells undergo further degeneration. If a drop of acetic acid be run under the cover-glass it will be found that the protoplasm of the pus cell is gradually cleared up, and as evidence of increased

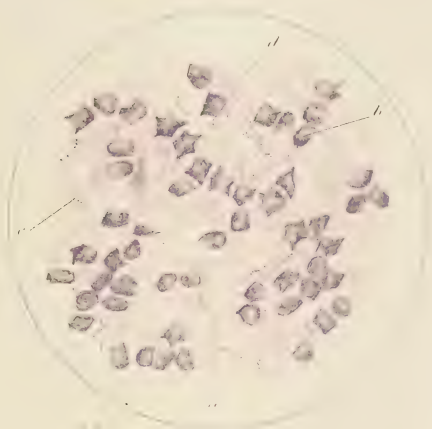


FIG. 27.—Pus from an acute abscess at time of evacuation. Dried, and stained with methyl violet. ($\times 700$.)

- a.* Pus corpuscles, between which may be seen the thin film of coagulated albuminoid material.
- b.* Pair of micrococci. Diplococcus.
- c.* Chains of micrococci. Streptococci.
- d.* Sets of four. Tetrads.

activity of the cell at some earlier period, it is now found that the nucleus has become divided into small fragments, usually three or four in number. The mononucleated cells are fewer in number.

In most pus, unless it be very liquid, small fragments of fibrous tissue may be distinguished, but these fragments are very irregular, and evidently form only a small part of the connective tissue of the area in which suppuration has taken place; there is also a quantity of finely granular material which does not readily take on stains, and

probably consists merely of débris, broken down cells, and dead blood plates. Chemically, pus is an albuminoid fluid holding in solution or suspended in it the original constituent materials of the tissues (more or less degenerated), the various salts and organic substances that these tissues contained, plus a large number of degenerating cells migrating and fixed, a number of micro-organisms, peptones, leucin, and other proteid derivatives which can only be looked upon as the result of the digestive action exerted on the tissues (*a*) by certain definite micro-organisms, and (*b*) probably by leucocytes.¹ It is somewhat difficult to determine how the microbes act, but it is now very generally accepted that certain micro-organisms have the power of attacking bruised or partially devitalised tissues; on these they are supposed to exert a kind of digestive action; they use them as food, and in growing and multiplying excrete or separate from these albuminoid materials, poisonous products which act either directly on the tissues, or are absorbed into the blood and lymph vascular system, whence they may act either on the nerve centres or on the organs by which they are excreted, especially on the kidney and intestine; they there set up irritation which may give rise to grave inflammatory changes. Numerous organisms have been described in various forms of suppuration, but the most important are Staphylococci: *Staphylococcus pyogenes aureus* (*Micrococcus osteomyelitis*), *Staphylococcus pyogenes albus*, *Streptococcus pyogenes* and *Micrococcus pyogenes tenuis*. Other organisms sometimes giving rise to or associated with suppuration are *Staphylococcus cereus albus*, *Staphylococcus cereus flavus*, *Pneumococcus*, *Bacillus pyocyaneus*, *Bacillus pyogenes fetidus*, *Bacillus coli communis*, *Bacillus lactis aerogenes*, *Bacillus aerogenes encapsulatus*, *Micrococcus tetragonus*, *Diplococcus intracellularis meningitidis*. Although many other organisms which appear to have a secondary pyogenic action have been found in certain specific diseases, such as gonorrhœa, typhoid fever, influenza, glanders, tubercle, leprosy, actinomycosis, etc., it is scarcely necessary to do more than mention them.

The dead leucocytes that are found in pus must be looked upon as the cells that have been brought up rapidly to interfere with the spread or diffusion of the products of the micro-organisms; a large number of these cells coming into contact with the poison in a concentrated form may succumb to its action, but before doing so they are able to deal with a certain quantity of this substance, breaking it

¹ For the composition of pus refer to any of the systematic text-books.

down and rendering it inert. Other cells are constantly being brought up to assist those that first come up, until at length the bacteria are completely hemmed in; they live for a short time on the dead tissues, but being localised first by the barrier of leucocytes and lymphocytes, and later by the actively proliferating cells, they ultimately die either

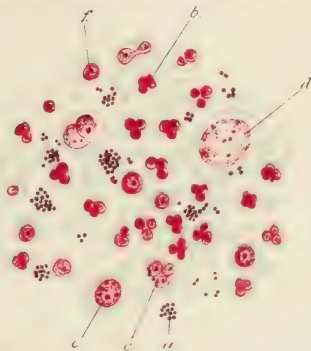


FIG. 28.—Pus from abscess in a case of acute periostitis with staphylococcic infection, *S. pyogenes aureus*. Stained by Ziehl-Neelsen's method and with light green. ($\times 1000$.)

- a. Bunches of staphylococci in the purulent fluid.
- b. Polymorpho-nuclear cells.
- c. Polymorpho-nuclear cells containing staphylococci.
- d. Large hyaline cell with ingested microphagocyte or microphage, and staphylococci—macrophage.
- e. Hyaline cell.
- f. Lymphocyte.

from inanition, or because they are poisoned by their own products. It is found, very frequently, on opening an abscess, that no organisms can be seen, those that were originally present appearing to have undergone degenerative changes, and to have been taken up and digested by the "phagocytes" or devouring cells.

SUMMARY OF PROCESSES OF REPAIR

230. If a collection of pus be not of very large size it may ultimately be absorbed; the leucocytes at the margin do part of the work, but the bulk of it is carried on by the larger mononuclear cells and fibroblasts, which, after some time, where foreign bodies are present,

appear to result from a process of proliferation. The wall of an abscess, in the later stages, may be looked upon as a granulating surface, similar in many respects to that of an ulcer, throwing off dead cells; the exudation of leucocytes from the vascular loops (formed by the proliferation of pre-existing endothelial cells, as possibly are also some of the large

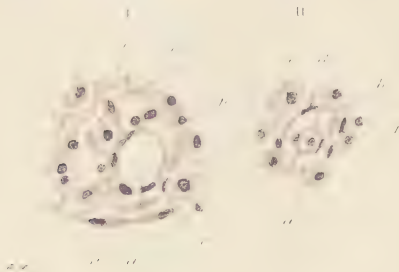


FIG. 29.—Young vessels from the granulation tissue of a healing wound. Stained with logwood and eosin. ($\times 450$.)

- I.
 - a.* Lumen of young vessel.
 - b.* Embryonic wall.
 - c.* Perivascular lymph space.
 - d,d.* Cells or buds shooting out from thickened mass of protoplasm and cells at one side of the vessel. These are probably derived directly from the pre-existing endothelial cells. It is from such buds that the new vessels are formed.
 - e.* Layer of cells forming outer boundary of newly formed perivascular space.
 - f.* Large plasma cell.
 - g.* Fibroblasts.
 - h.* Lymphocyte.
- II. Transverse section of a very young vessel.
 - a.* Lumen in which is a leucocyte.
 - b.* Wall of vessel (simply a couple of flattened endothelial cells).
 - c.* Rudimentary perivascular lymph space.
 - d.* Endothelial cell.
 - e.* Large connective tissue, fibroplastic, cell.
 - f.* Fibroblast.

mononuclear cells), and the proliferation of fibroblasts, are much the same in both cases; it is on the presence of these that healing depends after the pus has been evacuated or absorbed. The changes that occur in the connective tissue cells have already been referred to, and it appears that to them and the endothelial cells must be assigned the power of forming new tissue. The polymorpho-nuclear leucocytes may

play a very important temporary part, but it is that of scavenging ; some of the mononuclear cells, on the other hand, whilst continuing the scavenging process, and helping to remove the leucocytes that have already done their work, ingesting them and utilising them as food, have a further work to do ; those derived by proliferation form not only the new connective tissue, fibroblasts, but also the embryonic blood vessels, the new blood vessels being apparently nothing more than tubes formed of cells of endothelial type. The mere mechanical protrusion of vessels, on unsupported surfaces, may be an important factor in vascularisation, but there are certainly other and even more important processes which can usually be followed near the surface of a healing wound. Continuous with the cells which form the walls of the pre-existing minute vessels, single rows or small columns of cells appear to shoot outwards into the fibrinous lymph. Into these small columns the blood gradually makes its way as a channel or lumen is formed, between which and the original vessel communication is then maintained. In some cases this new vessel appears to be the result of a slow growth, the proliferation of the endothelial cells being always a little, but only a little, ahead of the advancing column of blood ; in others, however, it appears as though a single row of cells is first thrown out, this proliferating and gradually giving rise to a more complicated column, which, rapidly opening up, receives the blood. It is only when the surface is approached that this column of cells appears to give off lateral branches. After the branching commences loops are formed by the junction of the lateral processes ; the pushing out of loops in the manner in which it is usually described is not of frequent occurrence so far as can be made out from the examination of a considerable number of specimens, the transverse portion of the loop being formed at a comparatively late stage of vascularisation. Once formed, the vessels may give off other branches, but their walls gradually become more fully developed and the branches thrown out become fewer in number. In all these cases it is found that around the vessel there is usually a space, due, probably, to the alteration, from time to time, in the size of the vessel, and to the necessity that exists for some space in which may accumulate the fluid and cell elements that escape from the vessel. This perivascular lymph space is ultimately bounded by cells, which undergoing proliferative changes, are said to give rise in turn to lymphocytes, large mononucleated cells, plasma cells, and even endothelial cells

(§ 218). These cells certainly form the tissue from which perivascular lymphoid or adenoid tissue is developed. The walls of the vessels in an old healing wound are usually much thicker than are those of a recent one; this is due, apparently, partly to proliferation of the cells which form the intima, giving rise to what might be spoken of as an obliterative endarteritis, and partly to the proliferation of the fibroblasts of the external coat—periarteritis. Along with this thickening of the vessel wall, we see, as in the case of the healing ulcer (§ 225), in the deeper layers of the granulation tissue, numerous spindle-shaped cells, fibroblasts, which, running parallel to the surface, form a kind of interlacing network with the blood vessels; as these become older and develop into connective tissue they gradually contract, help to constrict the blood vessels, and so cut off a supply of blood, which is no longer necessary for the nutrition of the more fully developed fibrous and connective tissues.

It will thus be seen that all these inflammations and healing processes are very intimately bound up one with another. On serous surfaces, as already described, it is found that every step is merely preparatory to a succeeding one, and that in many, or even in most cases, temporary makeshifts are resorted to in order to prepare the way for the formation of more permanent structures. First, there is the dilatation of the blood vessels accompanied by softening of the cement substance between the endothelial cells and emigration of polymorphonuclear leucocytes, and perhaps lymphocytes, though these more probably are brought up along the lymphatics, or they may be the result of proliferation of the cells in the perivascular lymph spaces and (probably through this softened and spread-out cement substance) effusion of plasma; all this resulting from some injury or irritation to which the tissues are subjected, the various processes at this stage being set up in order to check or counteract the action of the irritant.

When these exudations and the fibrin formed from them have done their work and have localised the area of action of the irritant or injury, and have formed a sharp line of demarcation between the healthy and the abnormal tissues, they have no longer any function to perform, they are foreign bodies, and as such must be removed. Acting as foreign bodies, and along with the other irritants, they induce proliferation of the fibroblasts and endothelial cells; this is accompanied by the formation of blood vessels, which remain in existence so long as they are required, but then soon disappear; the process of healing

is now completed, and the tissues return as far as possible to their normal condition, though it usually takes a long time for the extra fibrous tissue to be absorbed ; in fact, it is doubtful whether complete absorption ever does take place.

If these facts are borne in mind, most of the processes of inflammation and healing in other organs may be readily enough understood, and it is because of their great importance in this respect that the general plan of a practical work has been departed from in order that attention may be drawn to them as early as possible.

CHAPTER IV

THE LIVER

231. The weight of the normal liver when taken from the body is about 3 lb. (1·36 kilogramme). It is covered by a smooth capsule, which has a glistening appearance, is of a bluish-pink colour, and is fully though not tensely distended. The glistening appearance is due

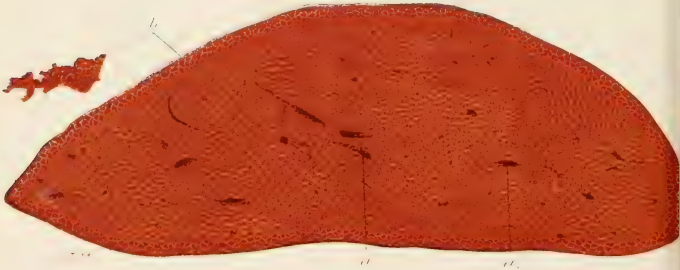


FIG. 30.—Section of a piece of almost normal liver in which there was only slight fatty infiltration, *a* (where the outlines of the lobules are more distinctly marked). The size of the lobules is here indicated.

- a.* Branches of the portal and hepatic veins, seen in transverse and longitudinal section.
- b.* Sections of lobules—approximate size.
- c.* Capsule of liver.

to the reflection of the peritoneum over the surface of the organ, and is not seen at the posterior border, where the peritoneum is absent.

Beneath the capsule, and through the delicate subcapsular tissue, the lobules or small subdivisions of the liver substance can usually be seen; they vary in size from about $\frac{1}{20}$ to $\frac{1}{16}$ of an inch (1·27 to 1·6 mm.) in diameter. The substance of the liver “cuts” easily, but is firm and close; the surface of a section of a healthy liver is of a dull chocolate

colour, and the outlines of the lobules are usually very indistinctly marked. The capsule is thin and delicate, and only here and there very fine bands of connective tissue may be seen passing from it into the deeper part of the liver substance. In the cut section a number of large openings, mostly branches of the hepatic vein, are seen. The gall bladder is usually semi-distended with a brownish-yellow bile which may be readily pressed through the common duct into the duodenum.

232. For the preparation of such a liver for microscopic examination, see §§ 57–62, 87, 102, and 195, and 103, or 110*b* and 132.

Examine in order—(1) the capsule and the inter- and intra-lobular tissue; (2) the portal vein; (3) the hepatic artery; (4) the hepatic vein; (5) the bile ducts; and (6) the liver cells, or parenchyma of the organ. Always keep to this order in examining sections of either the healthy or the diseased liver.

On the outer surface of the capsule of a liver, placed in the hardening fluid immediately after death, is found a layer of endothelial cells, the serous layer proper; beneath this is a layer of irregular connective tissue, in which are yellow elastic fibres, and, deeper still, a layer of lamellated connective tissue, merely a continuation of Glisson's capsule, which plays a most important rôle in perihepatitis and polylobular cirrhosis. Continuous with the subcapsular tissue are processes of similar lamellæ—with flattened branching connective tissue cells between—running at intervals into the substance of the liver, where they are found in the portal canals. In the human liver there is little or no connective tissue between the individual lobules, but running along with the larger branches of the portal vein is an appreciable quantity of this tissue. It may be stated at once that a study of a single lobule of the liver, and of a single portal canal, will give the key to the structure of the whole organ as usually described.

The portal canals are the large spaces seen in a section of the liver, in which are the openings of the branches of the portal vein. In each of these canals are found (see Fig. 31)—(1) A large opening (*v*), the portal or interlobular vein, which brings the blood from the alimentary tract to the liver. The walls of the vessel are comparatively thin. (2) One or two small branches of the hepatic artery (*a*) with thick walls. These, the nutrient arteries, have the same structure as have small arterioles in other tissues and organs. (3) Small bile ducts (*b*) in any

one of which the wall is of considerable thickness as compared with the lumen. Forming the inner part of this thick wall is a distinct layer of nucleated columnar epithelium.¹ These various structures are embedded in the connective tissue (*c*), which has entered the liver at the hilus, along with the vessels, and now leaves the portal canals to run in the smaller portal spaces, and sometimes even between the lobules, meeting the strands of tissue that come from the surface of the organ and forming a supporting framework for the liver substance proper. Examine a section through a lobule near the portal canal. It

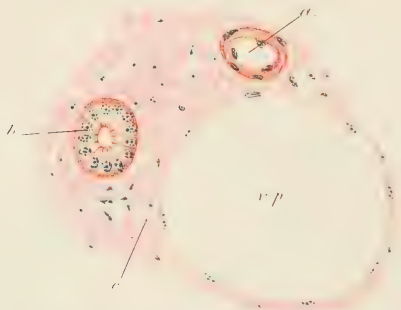


FIG. 31.—Section of portal canal, stained with alum hæmatein and van Gieson's stain. ($\times 200$.)

- v.p.* Section of the portal vein, with large lumen and comparatively thin wall.
- a.* The small branches of the hepatic artery, with thickened walls.
- b.* Sections of bile ducts, each with a regular layer of nucleated columnar epithelium and a small orifice.
- c.* Connective tissue, continuous with Glisson's capsule, supporting the various structures in the canal.

may be described as a mass of polyhedral cells arranged around a central (hepatic) vein. Piercing this mass of cells, and running from the portal vein, at the periphery, towards the centre, are numerous

¹ Remember the distribution of these vessels when the search for a lobule is entered upon. To find a lobule, look first for several portal spaces, which may be recognised by the fact that they contain *several* openings. Imagine lines drawn from these spaces to a common centre. Near this centre will be found a *single* opening—the hepatic vein, the centre of a lobule. The periphery of this lobule is marked by imaginary lines adjoining the several portal spaces running at right angles to those drawn towards the centre.

capillary vessels, said to be lined by a discontinuous epithelium, the individual cells of which are known as Kupffer's stellate cells. These have all the characters of actively phagocytic endothelial cells. The blood is thus brought into very close contact with the liver cells. Minot maintains that the blood comes into direct contact with the liver cells, and that as the endothelium does not form a complete layer, there is no basement membrane. There are no true lymphatics in this position,



FIG. 32.—Diagrammatic representation of the structure of a small portion of the liver, altered from Quain's "Anatomy."

- a.* Sublobular vein, into which the central veins, or hepatic venules (*b*) open.
- c.* Interlobular fissure, in which run the portal vein, etc.; running from the portal vein to the central vein are the portal capillaries, *d*.
- e.* The parenchymatous tissue, or gland substance proper, composed of masses of polyhedral cells.

and certainly no perivascular lymphatics. Between individual cells, or it may be at the angles between several cells, are the bile capillaries, which in their most minute ramifications are simply channels between adjacent liver cells, or actually within their substance (see §§ 232 and 241). These intra- and inter-cellular channels are continued into the smaller bile ducts, the epithelial cells of which appear to be derived from the same source as the liver cells.

The central veins of a group of lobules open into a larger branch

of the hepatic vein—the sublobular vein (Fig. 32). On transverse section through one of these groups of lobules the arrangement is diagrammatically represented in Fig. 34, in which the following structures are seen:—(1) Those situated at the angles between the lobules; and (2) the mass of liver cells perforated by the various structures already mentioned, including the hepatic or intralobular vein. For convenience of description this section of the lobule is mapped out into three distinct zones. These are—(1) The peripheral or portal zone, which, as its name indicates, is situated at the periphery of the lobule, and occupies one-third of the diameter of the section (area of fatty infiltration). (2) Within this is the intermediate zone, or, as it is sometimes named, the zone of the hepatic

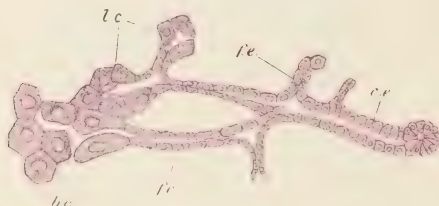


FIG. 33.—Commencement of biliary channels, and structure of smaller bile ducts (after Klein and Noble Smith).

- b.c.* Biliary canaliculi in the angles between adjacent liver cells.
- l.c.* Liver cells, slightly modified, just before the commencement of the bile duct proper, with its lining of flattened epithelium,
- f.e.* (intermediary portion of the duct).
- c.e.* Cubical epithelium of the somewhat larger bile duct.

artery, which, roughly speaking, also occupies one-third of the diameter. It is named the zone of the hepatic artery (area in which waxy degeneration is first met with) from the fact that the capillaries of the hepatic artery are supposed here to empty their contents into the portal *venous* capillaries which run between the inter- and intra-lobular veins. (3) And lastly, there is the central zone, or zone of the hepatic vein, situated in the centre of the lobule (area in which chronic venous congestion is first manifested). At the periphery of the lobule are the small branches of the portal vein, which empty their blood into the intercolumnar or portal capillaries. Klein holds that there are, in consequence of the mass of liver cells being *pierced* by the portal capillaries, short transverse columns of the liver cells

running at right angles to the radiating columns of the network of cells. The liver cells making up these columns are polygonal or polyhedral in shape, and have a granular appearance; as a rule, a single spherical or ovoid nucleus is to be observed, which stains deeply with carmine, etc.; a cell wall may also be demonstrated (Haycraft). Throughout the cell, granules of glycogen and brown pigment are



FIG. 34.—Diagrammatic representation of lobules of the liver, divided into zones.

p.c. Portal canal, in which are contained the following structures:—
b. Bile duct. *v.* Portal vein. *a.* Hepatic artery. *a.n.* Area in which chronic venous congestion is first manifested. *a.w.* Area in which waxy change is met with. *a.f.* Area of fatty infiltration. These three areas correspond to the central (*c.z.*), intermediate (*i.z.*), and peripheral (*p.z.*) zones.

present, whilst, in a liver removed from an animal killed shortly after food has been taken, globules of fat may usually be seen in the cells of the peripheral zone. The granular appearance of the cytoplasm is due to the existence of (*a*) an intracellular plexus, to be made out only with the aid of a very high magnifying power, and (*b*) secretion granules. An intranuclear network may also be seen. Herring and Simpson maintain that the cytoplasm "is pervaded by an irregular network of

fine canaliculi which in preparations of injected liver become filled with the injection material which has passed into them from the blood vessels." These intracellular canals often contain red blood corpuscles or blood pigment (Schaefer). The imaginary spaces at the margins of the lobules, joining the interlobular spaces, are spoken of as the interlobular fissures.

Sabourin maintains that the above description of the liver is not altogether satisfactory; he resuscitates the old theory, in support of which he was able to adduce considerable evidence, that the structure of the liver is essentially the same as that met with in other acinous glands. Delépine, as the outcome of independent anatomical and physiological observations, holds that the columns of liver cells are really tubes with a fine lumen, and that instead of being arranged around the terminal hepatic veins as above described, they form small pyramidal masses which correspond to the lobules of other glands, so that the centre of the lobule, as described by him, is the portal canal with its bile ducts, portal veins, and hepatic arteries; the columns of cells converging towards the bile ducts, and gradually becoming continuous with them. Near the portal space the diverging columns of liver cells are smaller, and have the character of intermediate tubes; further away from the portal space, *i.e.* in the intermediate zone as hitherto described, the cells are larger, whilst in the central zone they are again considerably smaller. Taking the centre of the lobule as at the portal space, and the interlobular fissures as occupying the position of lines drawn between the various hepatic veins, the above description might be repeated, simply changing the centre to the periphery,—the connective tissue forming the supporting framework in the centre of each lobule,—and we have an acinous arrangement of tubes all converging to a central collecting bile duct, the structure of the liver thus being brought into line with that usually ascribed to other acinous glands. A study of this arrangement enables us to understand many of the problems connected with secretion by the liver which, otherwise, are unintelligible. It may perhaps be held that it is difficult to recognise the arrangement of the tubes of a healthy liver, and this undoubtedly is the case, except when one set of them happens to be entirely in the plane of the section. We have to do with an organ in which there is so little interstitial tissue and in which there are so many confusing anastomoses that a section in such a plane can seldom be

obtained. A careful study of the grouping of the liver tubes will, however, show that Delépine's description is substantially accurate.

CLOUDY SWELLING OF THE LIVER

233. This condition is usually found in organs taken from patients who have died during the course of certain acute febrile conditions,

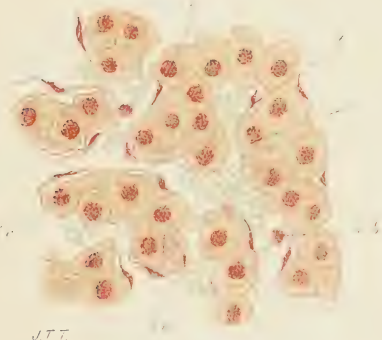


FIG. 35.—Cloudy swelling of the liver cells. Section stained in picro-carmin. ($\times 450$.)

- l.c.* Liver cells, swollen and granular; small globules are seen here and there, and the nucleus is slightly obscured.
- c.* Capillary vessels between the columns of liver cells; containing red blood corpuscles (green), and, *w.b.c.*, white blood corpuscles (carmin).
- e.* Endothelial cells forming the walls of the intercolumnar capillary vessels.
- f.* Kupffer's "stellate" cells (endothelial cells).

especially yellow fever, scarlatina, small-pox, and similar diseases, or those of septicæmic origin. It is also met with in the early stages of phosphorus, arsenic, antimony, alcohol, or sulphuric ether poisoning. It is really an inflammatory condition, and is described by Virchow as a parenchymatous inflammation. It is also spoken of as an early stage of acute molecular degeneration. (See Fatty Degeneration, § 251.)

On naked-eye examination the capsule of the organ is tense, the liver is swollen, though paler than normal (due to the diminished amount of blood in the *capillaries*), and, instead of having a clear

glistening appearance and firm substance, is somewhat opalescent and flabby. Harden (§ 58) and stain (§§ 102, 103, and 164 or 165).

($\times 50$).—The lobules are rather more distinctly outlined than usual, owing to a slight increase in the number of nuclei (due both to connective tissue proliferation and to migration) in the interlobular fissures; the capillaries are seen to be compressed by the columns of swollen liver cells (and by migrated leucocytes and lymphocytes).

($\times 450$).—The cells in the portal zone, where the change is always most readily seen, are distinctly swollen; they have lost their polygonal form, and have a much more rounded contour than have healthy liver cells; the protoplasm of each cell appears to be exceedingly granular and cloudy (this is probably due to an alteration in the thickness, or of the refractive index, of the rods which make up the intracellular plexus), and the nucleus is somewhat obscured. In some cases the cells are undergoing a process of division or breaking down; where this is far advanced the cell may consist almost entirely of a mass of granules, the nucleus having disappeared. On the addition of a drop of acetic acid to such a specimen, the granules disappear, the protoplasm of the cell becomes more homogeneous and transparent, and the nucleus resumes its normal appearance.

It is probable that here, as in the heart, cloudy swelling is often nothing but an early stage of fatty degeneration.

FATTY INFILTRATION OF THE LIVER

234. Fatty infiltration, lipomatosis, or adiposis of the liver cells, is found during the physiological process of digestion, and is only a pathological condition where there is an exaggeration and persistence of the normal periodic process. It may be due to the ingestion of excessive quantities of alcohol, or of such substances as fat, maltose, or sugar, or to defective oxidation and assimilation of these substances; but the essential factor in this condition appears to be that the fat is derived principally from without, and does not necessarily involve the breaking down of any protoplasm, though it is usually accompanied by impaired function of the cell, and may, ultimately, end in true fatty degeneration. It is met with in patients who have succumbed to phthisis, scrofula, cancer, and wasting diseases generally, and, as a rule, is unaccompanied by marked jaundice or ascites.

On naked-eye examination, the organ is enlarged, smooth, and

paler or yellower in colour than normal. The capsule is tense and glistening, and the anterior margin of the liver is considerably thickened and rounded. The tissue pits on pressure,—the indentation remaining for some time after the pressure is removed,—and is friable. The lobules are usually distinctly marked out, each having a pale yellow ring at its periphery, and a brownish-red or purple



FIG. 36.—Drawing of fatty infiltration of the liver (with fatty globules at the periphery of the lobule only). Stained with osmic acid. ($\times 50$.)

- a.* Transverse section of central or hepatic vein.
- b.* Portal canal with various openings.
- c.* Peripheral zone of a lobule, in which are the infiltrated and degenerated cells,—the fat globules are stained black with osmic acid.

centre: this may be seen even through the capsule. On section, the general pallor is distinctly marked, and the cut surface has a peculiar yellow mottled appearance. Though the actual weight of the organ may be considerably increased, the specific gravity may be so much diminished that a detached piece of the liver will not sink in water. When the surface is scraped droplets of oil readily recognised when

the scraping is floated on water—collect on the knife. Harden (§ 61 or 62), and stain (§§ 102 or 103, 135, 135*a*, and 170).

($\times 50$).—Examine a single well-defined lobule. In the early stages the infiltration is confined to the peripheral or portal zone,

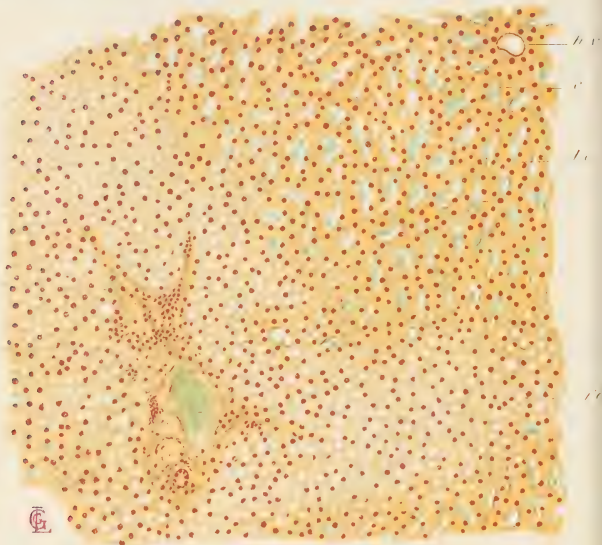


FIG. 37.—Drawing of portion of a lobule of a large fatty liver.

Section stained with picro-carmin. ($\times 100$.)

- h.v.* Central or hepatic vein.
- c.* Capillaries distended with blood.
- l.c.* Columns of healthy liver cells.
- f.c., f.c.* Liver cells in the peripheral zone in an advanced stage of fatty infiltration.
- b.d.* Small bile duct lined with cubical epithelium.
- v.p.* Portal vein distended with blood.
- c.t.* Connective tissue and bile duct in longitudinal section of an interlobular space.

that area in which the blood is emptied from the portal vein into the portal capillaries. The droplets of fat are usually large, though they vary greatly in size; in the more advanced stages they tend to run together, and to form large, clear, strongly refractile droplets, which appear to distend the liver cell, and push the nucleus to one

side. In very advanced cases the cells of the intermediate zone, or even those of the whole lobule, may be infiltrated; it is then difficult to distinguish the mass from ordinary adipose tissue.

($\times 300$).—The liver cells most affected, those in the peripheral zone, have lost their polygonal form, and are swollen and rounded. Each cell is made up of a thin film or wall of protoplasm, enclosing one or perhaps two or three droplets of fat (stained black by osmic acid). In the section stained with Sudan III. and hæmatein observe that at one angle of the cell, where the cytoplasm is thicker, is the nucleus, deeply stained, and standing out very prominently. The liver cell,

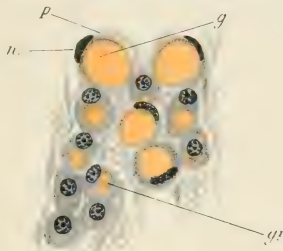


FIG. 38.—Cells from fatty liver (infiltration). Stained with Sudan III. and alum hæmatein. ($\times 300$.)

- p.* Thin film of protoplasm, forming, along with the nucleus, *n.*, all that is left of the proper substance of the liver cell.
- g.* A single large droplet of fat (orange), contained within the wall of protoplasm. It will be observed that the nucleus is distinctly seen, and is pushed to one angle of the cell, giving rise to the so-called “signet-ring” appearance.
- g'.* A cell containing two droplets of fat.

with its nucleus in this position and the thin film of protoplasm surrounding the globule of fat, is now said to have the appearance of a signet-ring. In consequence of the swelling of the cells, and of their being pressed together, their outlines or boundaries are often somewhat indistinct and obscured.

FATTY DEGENERATION OF THE LIVER

235. Fatty degeneration is to be looked for in the livers of patients who die during the course of wasting or exhausting diseases. It is also constantly met with as a sequel to cloudy swelling occurring in,

and following continued fevers, and the exhibition of those poisons already mentioned (§ 233), which act by interfering with the proper oxidation of the tissues. It is also met with in Addison's disease, in anæmias, and in phthisis, where, in addition to imperfect oxidation, there is decreased vitality of the tissues as a part of a general malnutrition. It is frequently seen in patients who have succumbed to malignant growths, especially cancer. Although it is impossible to draw a sharp line of demarcation between this and fatty infiltration, the conditions differ considerably in both naked-eye and microscopic characters, and, as they are met with under somewhat different conditions, it is convenient to treat of them under separate headings.

From the physical characteristics of the tissues, both naked-eye and microscopic, the liver when affected with fatty degeneration is known as the atrophic or wasted form of fatty liver. The organ, in the advanced stage of the process, and where a large number of the cells have become affected, is markedly wasted, both weight and specific gravity being diminished, and the capsule somewhat wrinkled. It is brown or brownish-yellow in colour, and on section the peripheral zone is usually paler than the remainder of the lobule; the tissue appears to be more or less opaque, and is friable, breaking down readily under the finger.

Harden (§ 61, 62, or 63), cut (§ 82 *et seq.*), and stain (§§ 102 or 103, 135, and 170).

($\times 50$).—The lobules are distinctly outlined, the liver cells are atrophied, and in the atrophied and somewhat angular cells are a number of small fat globules, each with a dark outline and a clear centre. These droplets of fat are usually said to be small, but there are several in each cell which may run together to form larger globules; they give the characteristic black reaction with osmic acid, and are often in greatest number near the periphery of the lobule; though, in some cases, the process extends throughout the lobule, and may be even more marked away from the periphery. The capillaries are usually dilated, and stand out prominently. In a picro-carmin stained specimen a number of migrated leucocytes may be seen as bright crimson points along the lines of the interlobular fissures, and in the interlobular spaces.

($\times 300$).—The cells are much shrunken, and have an angular outline. Scattered throughout the protoplasm of the cell are numerous oil globules, never of any great size; for, although some of them

may run together, they do not, as a rule, form a single large droplet unless the cell is much degenerated. Such of the protoplasm as remains is extremely granular, and the nucleus, when it can be made out, occupies the centre of the cell, though, in the majority of cases, it, like the protoplasm, is breaking down,—is undergoing pyknotic

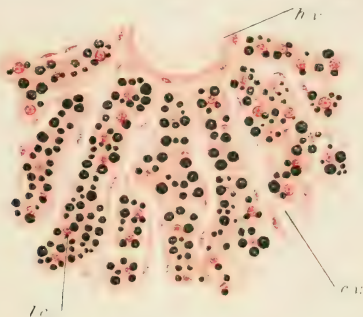


FIG. 39.—Drawing of liver cells undergoing fatty degeneration, taken from near the centre of a lobule. Stained with alum carmine and osmic acid. ($\times 200$.)

l.c. Liver cells arranged in columns. The outlines of these cells are very distinctly marked. The nucleus is visible in most of the cells, which are small, and have in their protoplasm several droplets of fat,—these droplets vary very much in size, but usually they are comparatively small.

h.v. Hepatic vein, the wall of which is slightly thickened.

c.v. Capillary vessels and delicate connective tissue, the nuclei of both of which are seen slightly stained by the carmine.

changes. In consequence of the atrophy, the outlines of individual cells are easily made out.

236. Where fatty degeneration has been brought on more rapidly, as in the case of phosphorus poisoning, the decrease in size of the liver is not so marked nor is the weight so much diminished; there are certain other characteristic features to which special attention should be paid.

The liver is pale, but at certain points—or it may be almost throughout the organ—patches of bile-stained tissue and small punctiform hæmorrhages, especially under the capsule, are usually seen. These are due to the rupture of the small bile ducts and arteries, the walls of which are found to have undergone fatty degeneration.

In consequence of the bile-staining, the whole organ is frequently of a canary yellow, or even a darker yellow, colour. On examination under the microscope, the protoplasm of the liver cells appears to be almost replaced by fat globules, which in this case are of considerable size—much larger than in ordinary fatty degeneration, as here there is no time for absorption of the fat to take place.

From the description given above it will be seen that it may sometimes be a difficult matter to determine whether we are dealing with a case of fatty infiltration or one of fatty degeneration.

It has been said that infiltration is due to the deposition within the cells of fat that has been derived from without, and that degeneration is due to the protoplasm of the cell itself supplying the material from which the fat is formed. In both cases there is incomplete oxidation, but the physiological occurrence of fat in the cells of the liver, after a meal, which may be taken as the type of the process of infiltration, and which results from the splitting up of proteids as the result of *metabolism* of substances from outside, has a very different significance from true fatty degeneration which results from the breaking down of the protoplasm itself—*internal metabolism*, or *katabolism* rather. This distinction, though useful for practical purposes, is no longer recognised as affording a complete explanation of what takes place by those who have given most attention to the subject.

As a matter of fact, however, we find that in fatty infiltration the greater part of the protoplasm of the liver cell is not destroyed; it, along with the nucleus which also remains active, is simply pushed aside to form a comparatively active film around the large fat globule, whilst in fatty degeneration there are evidently grave nutritive changes in the protoplasm—such of it as remains unconverted into fat, is extremely granular—and the nucleus, retaining its normal position, is evidently undergoing marked degenerative changes, as it does not readily take up any staining reagent. In the one case, if the fat is removed, both protoplasm and a normal nucleus may remain, whilst in the other, if the fat is removed, nothing but a small mass of granular protoplasm, with an imperfectly stained nucleus, is left.

WAXY LIVER

237. Synonyms, “Bacony” Liver, “Lardaceous” (*Lard*, Fr.), (*Speck Leber*, Ger.) “Waxlike,” “Amyloid,” “Albuminoid” Liver.

Waxy liver is met with in patients who have suffered from certain diseases in which suppuration has been profuse or of long standing. It is found, for example, in cases of chronic phthisis, especially where the discharge from the cavities, so characteristic of this disease, has been going on for some time, in empyæma, in bone disease accompanied by suppuration, and in syphilis, congenital or acquired, notably during the tertiary stages. It is also said to occur during the course of certain other diseases, such as chronic dysentery and leucocythæmia, and after acute rheumatism.

It is difficult to determine whether this is a true degeneration or simply an infiltration, as it appears to depend upon two sets of conditions—(1) Changes in the connective tissue elements, especially connective tissue fibrils and basement membranes; (2) an infiltration of these with certain unknown proteid materials, separated, apparently directly from the blood, in patients in whom *caseation* and *chronic suppurative processes* are going on.

Waxy liver derives most of its synonyms from some supposed physical resemblance to smoked ham, boiled bacon fat, and so forth. The organ is, in uncomplicated waxy disease, enlarged in all directions, is more square than usual, and the anterior margin is somewhat thickened and rounded, though not so markedly so as in the fatty liver. The capsule is smooth, glistening, thin and transparent, and so tense that the organ does not lie flat when placed on its anterior surface, the middle only coming in contact with the platter on which it rests, the edges being well raised. To the touch the substance is firm and hard, like a piece of indiarubber; it is indented with difficulty by pressure with the finger, and the indentation disappears almost as soon as the pressure is removed.

In advanced cases the fresh section has a firm sharp edge, and a peculiar pink colour, somewhat like that of smoked ham or salmon; the tissue is anæmic. A thin section is translucent, and its surface looks as though it were covered with a very thin layer of transparent gelatin.

On examining a lobule closely, in an organ in which the disease is not very advanced, it is usually possible to divide it, roughly, into three zones: the peripheral or outer zone, of a pale opaque yellow colour, forms a kind of outer ring; within this comes the intermediate zone, which is broader than the peripheral zone, and has the peculiar translucent appearance mentioned above; whilst within this again is

a zone which varies somewhat in colour, but is usually a little paler than the normal liver substance. This latter constitutes the healthiest part of the lobule.

Pour a watery solution of iodine (§ 133) over the fresh surface, and a selective staining is at once obtained. The translucent ring is stained a deep mahogany red or brown, the other zones assuming a canary yellow colour. This translucent or mahogany brown area is the



FIG. 40.—Section of waxy liver. Unstained. ($\times 50$.)

- a.* Capillaries of intermediate zone, which have undergone waxy change—glassy, translucent.
- b.* Small branch of hepatic artery.
- c.* Central or hepatic vein.
- d.* Liver cells of the peripheral zone, brownish-grey and opaque.
- e.* Angular, somewhat atrophied, opaque degenerating liver cells around the central veins. None of the liver cells are waxy.

portion of the lobule in which the lardaceous material is deposited. Harden (§ 60), and cut (§ 82 *et seq.*).

($\times 50$).—Examine an unstained section without a cover-glass, and note that in the intermediate zone of the lobule are columns of somewhat compressed liver cells, whilst between these are irregular, translucent, glassy-looking, or homogeneous streaks. These streaks, as will be found later, are the capillary vessels, the walls of which

have undergone waxy change. This hyaline or vitreous appearance is exceedingly characteristic of waxy liver, and once recognised can never be mistaken for anything else. The cells in the central zone appear to be comparatively healthy, whilst those in the peripheral zone are either healthy or are undergoing fatty infiltration; in both positions they can be readily recognised by their browner, more



FIG. 41. —Drawing of waxy liver, stained with iodine, and examined by reflected light. Lobule cut vertically. ($\times 70$.)

- w.* Capillaries in intermediate zone—waxy, stained dark brown.
- c.v.* Central or hepatic vein.
- v.p.* Small branch of portal vein.
- l.c.* Liver cells and unaffected capillaries in the peripheral zone, stained yellow.
- l.c'.* Liver cells and unaffected capillaries in the central zone.

opaque, appearance. Allow a drop or two of the watery solution of iodine to run over the specimen from one margin, and then examine it by transmitted light, when the liver cells in the central zone appear to take on a dark yellow or brownish-yellow stain, the fatty globules and liver cells in the peripheral zone are canary yellow, and the homogeneous streaks assume a deeper yellow tinge. Whilst

looking at the specimen, alter the angle of the mirror so as to turn off the light from below the stage; the homogeneous streaks now appear dark brown as when observed with the naked eye, and the liver cells previously dark are now yellow. Mount this specimen in the iodine mounting fluid (§ 133).

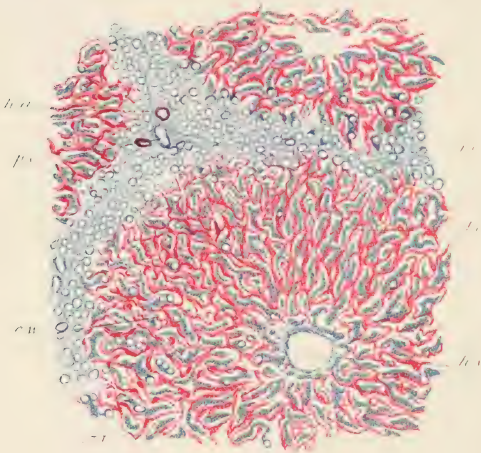


FIG. 42.—Drawing of waxy liver, stained with methylanilin-violet.
($\times 100$.)

- h.a.* Small branch of hepatic artery in portal space, middle coat waxy, stained red violet.
- p.v.* Portal vein.
- f.c.* Liver cells in peripheral zone (fatty infiltration).
- c.w.* Capillaries in intermediate zone—waxy.
- l.c.* Atrophied liver cells between waxy capillaries.
- h.v.* Central or hepatic vein.

($\times 300$).—In the liver cells are a few granules (glycogen) which take on the same staining as does the waxy material, for which, however, they must not be mistaken, as it is found that although glycogen gives the same reaction with iodine, when stained with methylanilin-violet (§ 117), it gives a blue reaction, by which it may be distinguished from the waxy material.

($\times 50$).—In a specimen stained with methylanilin-violet, the

homogeneous material has taken on a beautiful rose pink or red violet colour; the other tissues are slaty blue. This characteristic reaction defines most accurately and minutely the waxy tissues. In the portal spaces, the small arterioles of the hepatic artery are stained rose pink—this coloration is confined more especially to the middle coat of the vessel. In the intermediate zone of the lobule, where the change is most advanced, the cells are more angular than usual, are attenuated looking, and even under this power may be granular and atrophied; they seldom or never give a pink reaction, as they usually remain perfectly free from any waxy change, though they frequently undergo fatty infiltration and degeneration. In certain cases, especially where the waxy change has involved the capillaries of the peripheral zone, the wall of the portal vein may be similarly affected, in which case, of course, it gives the rose-pink reaction.

($\times 300$ or 450).—The arteriole in the portal canal is affected as follows:—The middle coat is picked out, and if a longitudinal section be examined, certain areas or bands only of this coat (not the muscle fibres, but the connective tissue fibrils between them) are seen to be affected. Later, the fibrous part of the inner coat becomes more or less involved, especially in its deeper layers, but the endothelial cells lining the vessel, although frequently granular and fatty looking, always give the blue reaction. If the branches of the portal vein are involved, the affection is similarly localised in the connective tissue fibrils between the non-striped muscle fibrils.

The capillaries in the intermediate zone are found to be the special seat of the waxy change. The walls are enormously thickened, and in many cases the lumen appears to be obliterated, so that little is to be seen but thick bands of translucent homogeneous material, stained a beautiful rose-pink, between which lie bands or rows of liver cells. These cells, atrophied and angular, are in many cases undergoing fatty degeneration; the nucleus is in its normal position, but is somewhat obscured, and the outline of the cell is distinctly marked; there is seldom any pink reaction to be seen in any part of the cell.

The capillary vessels in this position, simple though their structure is, are to be considered as being really made up of three coats—(1) a single layer of endothelial cells (the capillary wall proper) in immediate contact with the blood current; outside this is (2) a thin membranous or reticular structure, or basement membrane, composed of collagen fibrils, possibly with a few elastic fibrils; and (3) external to this again

connective tissue cells, the processes of which are connected with the basement membrane ; these are spoken of collectively as "perithelium." The waxy change takes place in the basement membrane or in the connective tissue filaments, between the two layers of cells. In some cases, however, it is extremely difficult to make out these perithelial cells, the swollen basement membrane apparently coming into direct

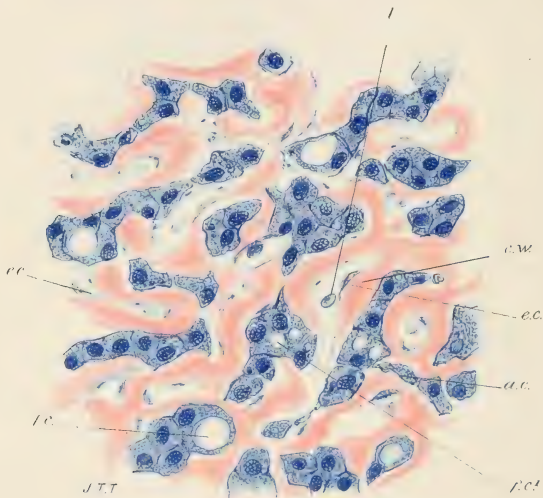


FIG. 43.—Drawing of waxy degeneration of liver. Methylanilin-violet. ($\times 450$.)

c.w. Walls of waxy capillaries, thickened, hyaline, red-violet.

e.c. Endothelium of capillaries, *not* waxy.

l. White blood corpuscle.

a.c. Atrophied liver cells.

f.c. Fatty infiltration of liver cells ; *f.c'*, smaller globules of fat in atrophied cells.

contact with the parenchymatous liver cells (as seen in Fig. 43). The delicate fibrils become enormously swollen, and ultimately so prominent that they overshadow the other structures. The endothelial cells are granular and fatty. This enormous thickening of the walls of the capillary vessels brings about two results,—one from the extension inwards,—gradual narrowing and, ultimately, complete obliteration of

the lumen of the vessel; another from the extension outwards—the compression of the columns of liver cells, leading to atrophy and molecular disintegration of the proper substance of the liver.

A third method of staining is to dip the section into a watery solution of iodine, and then convey it to a 4 per cent. solution of sulphuric or other mineral acid (§ 134). Virchow originally used a very strong acid. He also used a saturated solution of chloride of zinc for the same purpose. He describes the reaction as blue with the lardaceous material, and yellow with healthy tissues. The other methods, however, are more certain and more convenient, though it will be well to try this method where a delicate reaction is desired.

When the causes of waxy disease are compared with those which induce fatty and other changes of the liver, it will be readily understood why it is so frequently found complicated with fatty infiltration, fatty degeneration, tubercle of the liver, cirrhosis, and syphilitic scars. All these conditions, when present, modify the typical form of the waxy liver to a greater or less extent, a fact that must always be borne in mind when an examination of such a liver is being made.

CHRONIC VENOUS CONGESTION OF THE LIVER

238. Synonyms, “Nutmeg” or “Cardiac” Liver, “Cyanotic Atrophy.” Nutmeg liver is met with in cases where there has been cardiac disease, or extensive lung disease, such as emphysema, chronic phthisis (fibroid). It may be associated with any pressure on the inferior vena cava, or where there is obstruction to the return of the venous blood to the thoracic cavity. Where the primary lesion is in the heart, say at the mitral valve, a corresponding condition is found in the lungs, in the kidney, spleen, intestines, and in the portal system generally, so that amongst other symptoms during life may be diarrhoea, hæmorrhoids, chronic intestinal catarrh, varices, and ascites. The causes are, to a very great extent, mechanical: there is increased pressure in the hepatic vein, this pressure manifesting itself by its effects first in the central or intralobular veins, in the sublobular veins, and later in the intermediate and peripheral parts of the portal capillary veins, all this leading to enlargement of the liver. *On naked-eye examination* the capsule is tense, thin, and translucent; in the later stages the liver appears to be atrophied and tough, but still contains a considerable quantity of blood, which gives to the section a very dark red colour;

the capsule is thickened in patches, and may have on its surface (especially where ascites has been present) small villous growths—papillomatous growths, as they are sometimes incorrectly termed. The openings of the hepatic veins are enlarged, and therefore appear to be more numerous.

Examining a *lobule* in the earlier stages, it will be observed that it may be divided into three zones, each of which may be distinctly made out. The central zone is deep red in colour, and is engorged with blood ;



FIG. 44.—Early “nutmeg” liver, unstained. ($\times 70$.)

- h.v.* Central vein, dilated, walls thickened.
- c.c.* Dilated capillaries in central zone.
- l.c.* Pigmented and compressed liver cells in central zone.
- p.c.* Unaltered cells in peripheral zone.

the intermediate zone external to this is of a brownish-yellow tinge, the result of bile-staining, whilst the peripheral zone is pale and fatty looking. To this definite colour arrangement the term “nutmeg” is applied, and as the name refers simply to the appearance of the tissue, it is perhaps as good a one as can be used.

Virchow's name of “red atrophy” is given either to localised patches of congested tissue or, in the later stages of the disease, to the whole liver when it has become shrunken, and where the congestion extending throughout the lobule has done away with the nutmeg

appearance. Harden (§ 62 or 63). Mount (§ 195), one section unstained and one stained (§§ 102 and 195, also §§ 104 and 199).

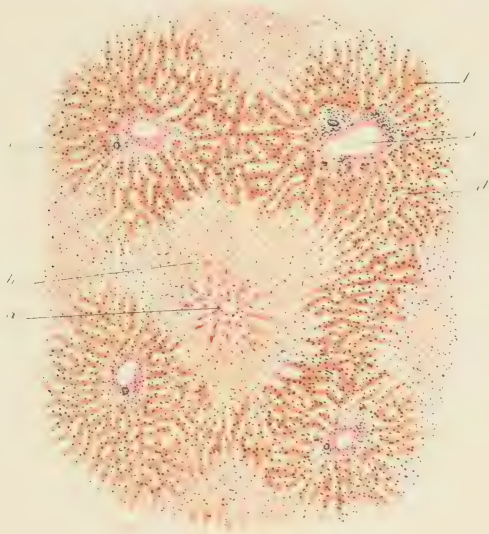


FIG. 45.—Section of "nutmeg" liver—advanced. Stained with alum hematein and picro-erythrosin. ($\times 50$.)

- a.* Dilated central (hepatic) vein, the wall of which is thickened and fibrous looking, with here and there some golden yellow pigment scattered in its substance.
- b.* Capillaries in the central zone, greatly dilated and filled with blood, with thickened walls similar in appearance to the thickened walls of the central vein. The liver cells between them have almost disappeared, being represented by a few pigmented granules.
- c.* Liver cells of the peripheral zone.
- d.* Capillaries in the peripheral zone, not greatly distended.
- e.* Branches of the portal vein, distended.
- f.* Bile ducts, lined with more or less cubical nucleated epithelium.

($\times 50$).—The central or hepatic vein is considerably dilated, and the lobules are distinguished much more readily than in the normal liver.

The capillaries leading to this central opening are also dilated, and are frequently filled with blood. Between the dilated capillaries the

liver cells are atrophied, angular, compressed, and granular looking, and, in the immediate neighbourhood of the central vein, contain granular masses of brown or orange-red pigment.

($\times 300$).—The walls of the dilated vein and its surrounding capillaries may be considerably thickened; in some cases they form distinct fibrous bands and circles. The pigment in the cells situated in the central part of the lobule is seen much more distinctly in the periplast of the cells, and does not obscure the nucleus, unless the cell is entirely filled with the colouring matter. The shrinking and atrophy of the liver cells are very marked, and in some cases small fat globules are seen lying scattered throughout the angular mass of protoplasm which represents the cell.

The atrophy of the liver cells is due to the distension of the capillaries; as these vessels become swollen, varicose, and tortuous, they compress the columns of liver cells between them, interfere with their nutrition, and induce an atrophic condition. In the later stages, the liver cells may have disappeared from the immediate neighbourhood of the central vein, and there is left simply a cavernous structure, made up of the fused walls of capillary vessels, which now form bands of fibrous-looking tissue, with the spaces between filled with blood.

In certain cases bands of fibroid or hyaline tissue, continuations of the fibroid vascular walls in the central zone, run to the periphery, and so cut up the lobules into distinct segments. Along with this hyaline thickening there is sometimes an apparent increase in the amount of connective tissue in the interlobular spaces and fissures. This gives rise to a form of cirrhosis, peculiar to the nutmeg liver, which is often seen in the later stages of the disease. This must be associated with the increased number of cells (proliferative) seen in the interlobular spaces and fissures, described as occurring in the earlier stages of the congestive process.

In the peripheral zone, well-marked fatty infiltration is often met with; the presence of this is probably accounted for by the slower passage of the blood through the portal system, in consequence of the obstruction to the outlet of blood from the hepatic vein, which brings about the following:—

As a result of the obstruction to the outlet of the blood from the vena cava, the hepatic vein cannot get rid of its contents so readily as under normal conditions; in turn the obstruction is felt in the sublobular, the central or intralobular veins, the intercellular capillaries,

and lastly, in the portal vessels; there is, in fact, in all these positions a partial stasis of the blood. In addition to this the liver cells, somewhat compressed and hampered by the increased pressure from the dilated and thickened capillary vessels, have their nutritive activity impaired, and various atrophic and degenerative (fatty) changes ensue. It is evident, too, that the red blood corpuscles, owing to the increased pressure within the venules, are much more prone to find their way into, and accumulate, in the "sinusoids," there to undergo disintegrative changes, which result in the separation and deposition in the liver cell of the colouring matter of the blood.

COMMON CIRRHOSIS OF THE LIVER AND PERIHEPATITIS

239. Synonyms, "Gin-drinker's" Liver, "Hobnail" Liver, "Polylobular Cirrhosis," "Coarse Cirrhosis," "Alcoholic Cirrhosis," "Granular" Liver.

In this condition, especially in its later stages, the liver is considerably diminished in size. It is firm to the touch, and its consistence may be compared to that of a piece of soaked leather. On the surface of the organ are a number of small projections about the size of the head of a "hobnail" or "tacket," and between these are distinct depressions or fossæ. On section, the deeper layer of the capsule—Glisson's capsule proper—is more or less thickened and opaque, the whole organ is usually yellow, and much paler than normal, the pallor being always most marked in the fossæ or depressions between the projecting hobnail-like nodules. The tissue is firm and tough, greyish-red gelatinous-looking bands of fibrous tissue being seen running in various directions throughout the substance of the organ, cutting it up into a series of areas of parenchymatous cells. These areas are of various sizes, usually from one-sixth to a quarter of an inch (5 to 7 mm.) in diameter; they are of a tawny-yellow colour, as a result of bile-staining; hence the name. As a rule, the cells of several lobules are grouped together, each mass or collection of lobules being bounded by one of these bands of fibrous tissue.

The fibrous bands near the surface are continuous with the deeper thickened layer of the capsule, into which they run at the point of depression around the hobnail elevation, and it is owing to the contraction of these bands that the elevations and depressions are formed, the former consisting apparently of a yellowish-brown mass of liver

cells, which is pushed by the contracting fibrous bands in the direction of least resistance, *i.e.* to the surface.

Harden (§ 60, 62, or 63) and stain (§§ 102 or 103, 110*b*, 132, and 126).

($\times 20$).—At the margin of the section the thickening of the capsule

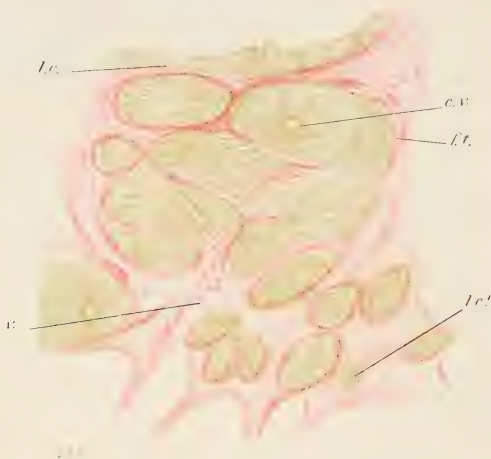


FIG. 46.—Drawing of a section of common cirrhosis of the liver.
Stained with picro-carmin. ($\times 20$.)

- f.t.* Bands of newly formed fibrous tissue running into the substance of the liver, and cutting it up into masses of cells of various sizes.
- l.c.* Indicates the margin of a mass consisting of a number of lobules.
- l.c'*. Indicates a portion of a lobule surrounded by newly formed fibrous tissue.
- c.v.* Central vein of a lobule.
- v.* One of the newly formed vessels, supplying the fibrous tissue with blood from the hepatic artery.

is seen as a mass of fibrous tissue, from which bands of different sizes may be observed running down into the liver substance from the lowest parts of the sulci. Between these fibrous bands are masses of liver cells, made up of six, eight, or ten lobules, corresponding in position to the elevations above mentioned.

The fibrous bands run along with the *medium-sized* branches of the *portal vein*, some of which are apparently slightly diminished in size by the pressure of the newly formed tissue around them. It is often difficult to distinguish the individual lobules, as there is, especially in the earlier stages of the disease, no increase in the tissue in the smaller interlobular spaces and fissures, whilst, owing to the pressure exerted by the contracting fibrous bands in the larger portal spaces, the lobules are so pressed together that the central vein may be partially obliterated.

($\times 300$).—In the newly formed bands of fibrous tissue are enormous numbers of rounded extravasated polymorpho-nuclear leucocytes and lymphocytes and fibroblasts, each with a nucleus, and surrounded by a small envelope of protoplasm. Amongst these are other cells of larger size, mononuclear cells, many of which are apparently the result of proliferation. In the later stages it may be observed that the number of round nuclei is apparently much diminished, whilst in place of them appear (according to the method of staining) pink or delicate blue bands of fibrillated tissue; scattered at intervals through this are numerous elongated nuclei,—the nuclei of flattened fibroblasts,—around which a fibrillated periplast has been formed. The more advanced the disease, and the more contracted the organ, the more fibrous does this fibro-cellular tissue become, until in some parts it may be represented merely by a band of contracting cicatricial tissue. This fibrous tissue in some cases, however, is exceedingly vascular, a vascularity which by injection may be proved to be due to the formation of new capillaries and small vessels, which derive their blood supply from the pre-existing small branches of the hepatic artery. These new vessels, embryonic in character, often consist of mere channels lined by a single layer of endothelial cells, and are frequently filled with blood, especially if the tissue has been preserved in Müller's fluid. Hence, if a fresh "cirrhotic" liver be injected with a fine injection mass—carmine, say—the bands of fibrous tissue become deeply coloured.

The bile ducts are probably unaltered in number, though *relatively* they appear to be more numerous and of greater calibre. In the logwood-stained specimen they are seen, in longitudinal section, as double rows of nuclei; but in the "Benda" and picro-carminic stained specimens both nuclei and protoplasm of the epithelial cells lining the smaller ducts may be readily made out.

The masses of cells, composed of groups of lobules, are, at all

points, somewhat closely pressed together, the cells sometimes containing globules of fat, the result of altered vascular relations and pressure-malnutrition.

At the periphery of the masses of lobules, thin bands of fibrous or fibro-cellular tissue may be seen shaving off layer after layer of liver cells, the size of the groups of lobules being thus gradually cut down.

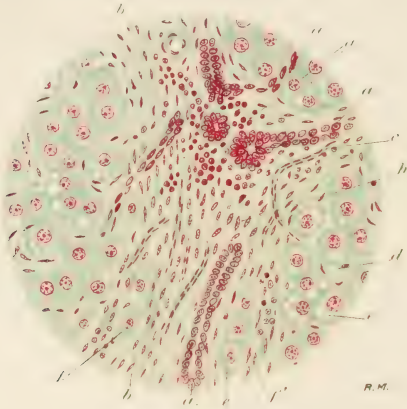


FIG. 47.—Section of common cirrhotic liver ($\times 350$), stained with Benda's stain, in which are three masses of liver cells; between these is a band of fibrous tissue running in the portal space.

- a.a.* Small bile ducts lined by epithelial layer.
- b.* Nuclei of connective tissue corpuscles.
- c.* Newly formed blood vessels, supplied by the smaller branches of the hepatic artery.
- d.* Sections of intercolumnar or portal capillaries.
- e.* Globules of fat in the compressed and degenerating liver cells.
- f.* Single liver cells, and *f'*. small masses of liver cells "shaved" from the main mass by ingrowing connective tissue cells.
- g.* Leucocytes—polymorpho-nuclear cells and lymphocytes.
- h.* Fibroblasts.

The cells so cut off and compressed between the layers of fibrous tissue soon lose their nuclei, and become flattened and angular, the protoplasm of the cell becomes granular, and sometimes contains droplets of fat or pigment granules. Eventually these cells disappear. The cutting off of these thin layers of liver cells is very characteristic of the polylobular form of cirrhosis.

To sum up: the change consists essentially in an increase of the fibrous tissue in Glisson's capsule. This may commence as a perihepatitis or inflammation of the superficial part of the capsule. In time prolongations from it run along with the larger or medium-sized branches of the portal vein, as a result of the extension of a chronic inflammatory process along these lines. The branches of the portal vein in these spaces become constricted as the connective tissue increases around them, with the result that the larger branches of the portal system become dilated, and great dropsical effusion may ensue. This continues, unless, or until, an anastomotic venous circulation is

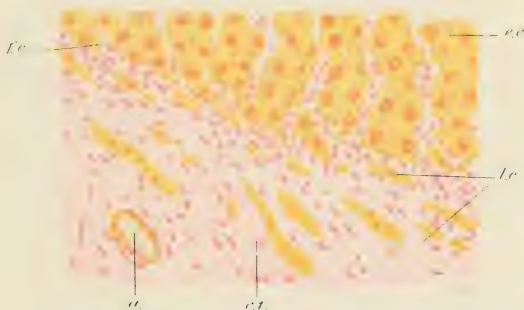


FIG. 48.—Section of common cirrhosis of the liver, stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- e.c.* Columns of liver cells at the margin of a group of lobules.
Between these columns young connective tissue is seen.
- f.c.* Liver cell infiltrated with fat.
- l.c.* Atrophied and flattened liver cells shaved off from the main body by the encroaching connective tissue, *c.t.*
- a.* Small branch of the hepatic artery.

set up—(1) through the veins in the suspensory ligament and around the obliterated umbilical vein,¹ or (2) through new or distended veins in the thickened capsule.

The biliary passages are little affected, and jaundice seldom makes its appearance until the very late stages of this condition. The lobules are pressed together, and their outlines are lost. The liver cells undergo degenerative changes.

There is a less common form of alcoholic cirrhosis, in which the organ is greatly enlarged; the naked-eye appearances are much like

¹ "Traité d'anatomie descriptive," par Ph. C. Sappey, p. 341.

those met with in the following, or biliary, form ; but we find that the distribution of the connective tissue is not so regular, the liver parenchyma is cut up into masses of very various sizes, and in the cells marked fatty degeneration and infiltration are met with. The splitting off of cells from the periphery of the masses points to the fact that here the disease advances rapidly and is similar to, but more advanced than, the common form. The biliary form of cirrhosis may sometimes be simulated, the new fibrous tissue then running into the substance of the lobules, where new bile ducts are formed.

ACUTE INTERSTITIAL HEPATITIS

240. If a section of a cirrhotic liver be examined in the later stages only, it is difficult to understand the exact nature of the process, but if, at the same time, we can examine a section of a liver taken from a case of some such disease as small-pox, measles, scarlet fever, typhoid or other specific fever, in which a marked cellular infiltration occurs in the portal canals, and sometimes even along the course of the intercolumnar capillaries, we may often derive material assistance to our understanding of the sequence of events. There is evidently advanced cloudy swelling of the parenchyma of the organ ; moreover, it may be noted that in the portal spaces, in which there is undoubtedly an increase of blood, there are usually peculiar grey or red gelatinous-looking points, the interpretation of which can only be given after a careful microscopical examination. Harden (§ 62 or 63) a piece of a liver in which the above appearances are presented from a case of one of the diseases named ; stain (§§ 102 or 103, 110*b*, and 126 or 162), and mount (§ 195 or 199).

($\times 50$).—Note the evidences of cloudy swelling of the parenchymatous cells (§ 233). In the medium-sized and smaller portal canals, and sometimes along the portal fissures may be seen a large number of deeply stained nuclei, evidently those of polymorpho-nuclear leucocytes emigrated from the vessels, or of proliferated fibroblasts, or of both. These masses of cells (the grey gelatinous points above mentioned) appear to be more intimately associated with the branches of the portal vein than with the other structures in the portal canals, and their distribution coincides almost exactly with that of the connective tissue seen in the commoner forms of cirrhosis.

($\times 300$).—Note the cloudy swelling of the liver cells, the distinct walls of the capillary vessels (Kupffer's stellate cells) in the portal zone,

and the increase in the number of polymorpho-nuclear and hyaline leucocytes and lymphocytes around the vessels in this area. In the portal spaces the emigrated and proliferating cells are very numerous; the columnar epithelium of the bile ducts is slightly more granular than usual, but otherwise these marked inflammatory changes have affected

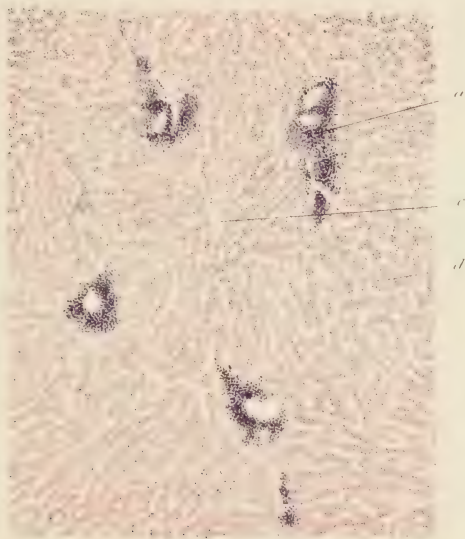


FIG. 49.—Early acute interstitial change in the liver of a patient who died from scarlet fever. Section stained with eosin and logwood. ($\times 50$.)

- a.* Small portal spaces in which the interstitial changes are well marked—cell emigration and proliferation.
- b.* Interlobular fissures in which similar new cellular tissue is seen.
- c.* Hepatic vein.
- d.* Liver cells, swollen and somewhat cloudy.

the bile duct in a relatively slight degree. The portal veins with their thin walls are evidently somewhat compressed by the large amount of new tissue surrounding them. From the commencing fibrillation of the protoplasm of the cells (the nuclei of which come out so prominently), it is evident that even here the process of connective tissue formation has already begun, and it must be assumed that many of the

large rounded or elongated nuclei seen are those of proliferating fibroblasts. If now we consider that this formation of fibrillated tissue has gone on still further, as it undoubtedly does in more chronic cases, we

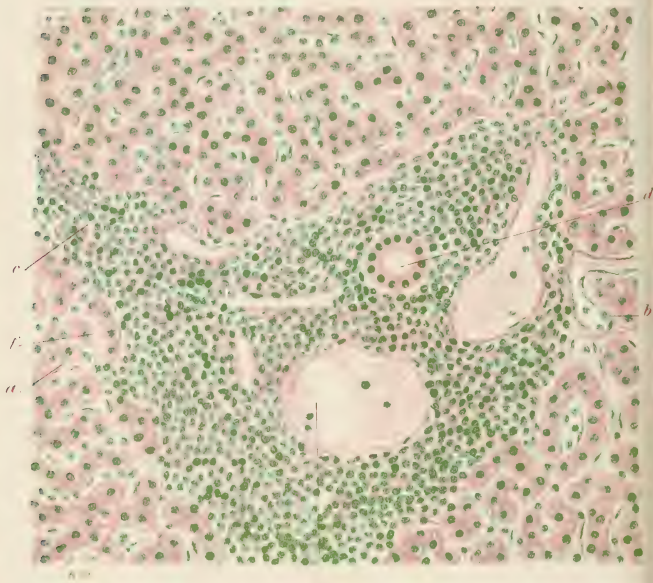


FIG. 50.—Early acute scarlatinal interstitial hepatitis. Section stained with methyl-green and fuchsin. ($\times 300$.)

- a.* Liver cells in a condition of cloudy swelling.
- b.* Intercolumnar capillaries with distinct walls (Kupffer's stellate cells), and containing numerous leucocytes.
- c.* New tissue in portal space, traces of fibrillated tissue to be seen.
- d.* Small bile duct with well-formed columnar epithelium.
- e.* Branch of portal vein.
- f.* Small branch of hepatic artery.

can see that this acute inflammatory interstitial hepatitis, with its accompanying acute parenchymatous changes, may gradually pass into the cirrhotic stage, in which the contraction of the fibrous bands, interfering with its nutrition, with the vascular supply of the liver tissue, and also,

by actual pressure, may gradually give rise to the features so characteristic of common chronic cirrhosis. It should be noted, however, that there may be very similar appearances in the early stages of acute abscess formation in which the new cellular tissue, in place of going on to fibrous tissue formation, becomes disintegrated, probably owing to the presence of pus-forming micro-organisms. The abscesses formed under these conditions differ but little, if at all, either in position or in structure, from the typhoid lesions to be afterwards described (§ 250). Bear in mind the above condition when considering the following.

"BILIARY" CIRRHOSIS

241. Synonyms, "Hypertrophic (?) Cirrhosis," "Monolobular Cirrhosis," "Hyperplastic Fibroid Degeneration."

Naked-eye appearances.—The liver is usually increased in size, the surface is finely granular, like a piece of morocco leather, and the substance of the organ is hard or even brittle. On section the parenchymatous tissue may be bile-stained in patches, of different hues (yellow to dark green), or may be pigmented or blood-stained, the fibrous tissue remaining grey or greyish-red. It is often extremely difficult to make out where the fibrous tissue ends and the parenchymatous substance begins, as the young fibrous tissue now passes round, and encloses, individual lobules. The portal veins may, in some cases, though not usually, appear to be distended.

Harden (§ 59, 61, 62, or 63), stain (§§ 102 or 103, 110/ and 126 or 162), and mount (§§ 195 or 193 and 199).

($\times 50$).—The capsule is not necessarily greatly thickened; but in the small portal or interlobular spaces and in the interlobular fissures there is marked increase in the amount of new cellular or fibro-cellular tissue. There is, in fact, an interlobular or monolobular cirrhosis.

In the newly formed tissue are a number of double rows of nuclei, which evidently belong to the epithelial cells of the small bile ducts. These bile ducts are apparently much increased in number, and where the disease is advanced they are seen running along with the new fibrous tissue into the substance of the lobule. This increase is not so great as at first sight appears, as even in the normal condition bile ducts run for some distance into the lobule, where, however, they are not readily distinguished. The fibrous bands, running at right angles to the periphery of the lobule, may encroach upon it from all sides,

and split up the lobule into small masses of cells, which first becoming atrophied may ultimately disappear.

($\times 300$).—The connective tissue resembles that found in common cirrhosis, but appears to be formed from the fibroblasts associated with the walls of the smaller bile ducts rather than from those around the



FIG. 51.—Section of liver in which biliary cirrhosis, accompanied by jaundice, has been developed. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- a.* Mass of new fibrous tissue in which may be seen
- b.* A bile duct filled with dark bile pigment.
- c.* Smaller bile duct at the margin of a lobule, where there is a kind of transition stage between the liver cells and the epithelium of the bile ducts.
- d.* Normal liver cells.
- e.* Young cellular tissue where there is an increase of interstitial tissue.
- f.* Liver cells with infiltrating fat globules.

branches of the portal vein. Even the larger branches of the bile ducts are constricted by the proliferating and contracting tissue; in consequence of this there is increased pressure in, and slight distension of, the smaller branches. These small bile ducts also appear to be much more numerous at those points where the connective tissue

invades the lobule from its margin. Near the advancing portion of the newly formed bile ducts the liver cells appear to undergo atrophic changes, their nuclei divide, and the cells split and become flattened.

A somewhat minute description of the structure of the bile ducts, commencing at the larger branches and passing backwards, may here be appropriate.

The largest bile ducts are lined by a layer of well-formed columnar cells (Figs. 31 and 50), external to which is a limiting membrane, or *membrana propria*, probably composed of endothelial cells; surrounding this again is a coat of non-striped muscle fibre. The lumen of each of these tubes is large, and after death its walls are thrown into folds by the contracting muscle fibre. The smaller bile duct has a comparatively thick wall and small lumen; the epithelial cells are not so distinctly columnar, and are surrounded by no muscular coat. At or in the margin of a lobule the small ducts are much branched; the epithelial cells form a single flattened layer, but there is still a distinct *membrana propria*. This, the intermediary portion of the duct, opens directly and suddenly into the bile capillaries, which appear to consist simply of channels formed by the apposition of the grooved surfaces of several liver cells. Thus, a bile capillary is generally placed at the angle between three or four liver cells, a groove or depression in each cell forming its share of the capillary channel; still more minute channels run in the substance of the liver cell. It is much easier to understand the mode of formation of the new bile ducts if the structure of these normal bile ducts be thoroughly grasped, and if we assume that they are in the centre of the lobule, and not at its periphery as usually described. In the coarse new connective tissue, as it penetrates the periphery of the lobule, the liver cells are divided and flattened, and, quite close to, and continuous with, the columns are the small bile ducts running for some distance into the lobule, so that it may be safely concluded that the new bile ducts are formed from the splitting up of these liver cells,—by a process of division of the nucleus and then of the cell,—followed by further subdivisions,—until in place of the three or four cells surrounding the bile capillary, there are numerous small flattened cells resembling those around the smaller bile ducts; the process consists, in fact, of a reversion of the liver cell to its embryonic or epithelial type.

The condition is due in all probability to an inflammatory change set up around the branches of the bile duct, either by some chemical

irritation, or by irritation caused by obstruction to the outflow of the bile from the ducts.

In certain cases monolobular cirrhosis may be set up by a peri-

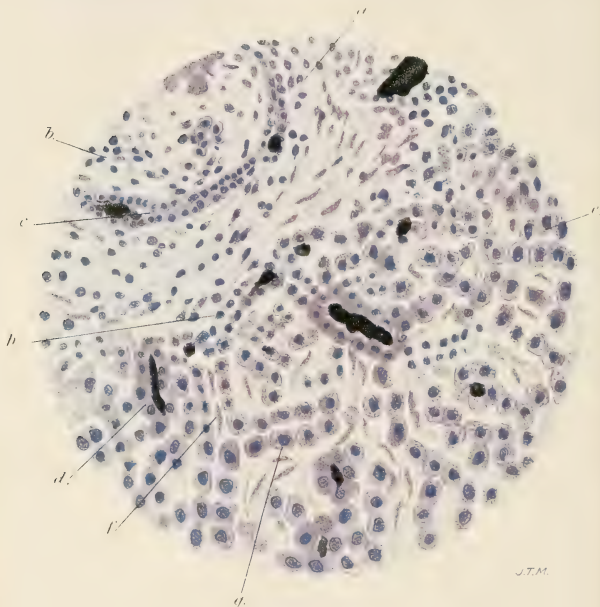


FIG. 52.—Section of liver, in which biliary cirrhosis has been developed. Stained with logwood. ($\times 300$.)

- a.* New fibrous tissue.
- b.* Imperfectly developed new bile duct in new tissue.
- c.* Well-formed bile duct, previously existing, containing pigment or inspissated bile.
- d.* Column of liver cells, now converted into a channel containing altered bile.
- e.* Normal or slightly cloudy liver cell.
- f.* Modified liver cells, intermediary portion of bile duct between ordinary liver cells (*g.*) and bile duct proper (*b.*).

phlebitis; but this form is much less common, and appears to be unaccompanied by any new formation of bile ducts.

From the above short descriptions of some of the forms of interstitial hepatitis it will be evident that they are due to the action of

some irritant matter conveyed by the blood vessels or contained in the bile ducts. In the common alcoholic form it would appear that the irritant is carried along the portal vein, the characteristic changes taking place along the course of the medium-sized branches of this structure; in other cases, however, the irritant may be conveyed, not by the portal vessels, but from the systemic arterial circulation, in which case the new tissue is developed around the finer branches of the hepatic artery; we then have a much finer cirrhosis than in the previous case. Lastly, the new growth may be due to irritation of the tissue along the course of the bile ducts—catarrhal inflammation and obstructed excretion by these channels apparently preceding this form. It is found that between, or of, these three forms there may be various intermediate stages or combinations. It has also been observed that the parenchymatous tissue is affected both primarily and secondarily, so that during the earlier stages we may have all the characteristic signs—cloudy swelling, etc.—of an acute inflammatory process in the parenchymatous cells before the interstitial changes are well marked; whilst in the later stages, owing to the interference of the connective tissue with the vascular supply, or with bile excretion, further degenerative or atrophic processes may supervene.

It is usually assumed that it is possible to draw a sharp line of demarcation between these various forms, and that definite atrophic or hypertrophic conditions of the liver are invariably met with. It must be borne in mind, however, that the hypertrophic form is simply the result of a widely diffused increase of connective tissue, where the amount formed is more than sufficient to make up for the atrophic and degenerative changes that take place in the parenchymatous cells, *i.e.* although there is a large increase of connective tissue, this does not affect the nutrition of the liver cells so profoundly as to induce their degeneration, death, and removal more rapidly than the connective tissue is formed. In the atrophic forms which are usually more chronic, the connective tissue is usually not so widely diffused, but it interferes so seriously with the nutrition of the gland cells of the liver, that they undergo atrophic changes more rapidly, and in greater proportion than, the new connective tissue is formed: of course the more acute and the more widely diffused the interstitial process the greater apparent hypertrophy there will be, whilst the more chronic and the greater the interference with the nutrition of the liver cells the more marked will be the atrophy.

It will thus be seen that, although we cannot distinguish sharply or give any clinical signs and symptoms by which it is possible to differentiate absolutely between the above forms of cirrhosis, it is nevertheless true, generally, that where the branches of the portal veins are specially involved, we shall probably find dropsy and the associated conditions, and that where the bile ducts are affected, jaundice may be looked for. The following list of comparative differences, then, must be accepted as having only a general application. It may, however, prove useful in drawing attention to the different forms, it being distinctly borne in mind that there are hypertrophic forms of cirrhosis in which the branches of the hepatic artery, rather than the bile ducts, appear to be the structures around which the interstitial changes are specially localised.

IN COMMON CIRRHOSIS

1. The bile ducts appear to be but little involved in the growth of connective tissue, there is little or no jaundice or bile-staining of the liver tissues, and few new bile ducts are found on microscopic examination.

2. In consequence of the new growth of tissue taking place along the course of the portal veins, especially the medium-sized branches, ascites is a very common complication, as are also hæmorrhoids, varicose conditions of the veins of the œsophagus, and congestion, or even hæmorrhage in the gastro-intestinal tract.

3. In the early stages, in consequence of the increased amount of young connective tissue in the portal spaces, there may be considerable enlargement of the organ; but later, where this tissue is becoming fibrous but cicatricial and contracting, there is usually a considerable diminution in the size of the liver.

4. The liver is rough, with projections, about the size of a hobnail, on its surface. The capsule is thickened and opaque, especially at the bottom of the fossæ or sulci which surround these projections.

5. The masses of liver cells vary very much in size, some consisting of several

IN BILIARY CIRRHOSIS

1. The structures around the bile ducts are those first involved, the jaundice and bile-staining of the liver substance are, as a rule, well marked, and there is a well-marked formation of new bile ducts.

2. The portal veins are not so frequently involved, and ascites, hæmorrhoids, etc., are rare.

3. In consequence of the large amount of new tissue diffused throughout the liver, it is considerably increased in size, the increase of new tissue being greater than the atrophy of the parenchymatous tissue.

4. The surface of the organ is smooth (morocco leather feeling), and the capsule is not so markedly thickened.

5. The masses of liver cells consist of single lobules, which, however, are con-

IN COMMON CIRRHOSIS—*continued*

lobules, whilst others are smaller than a single lobule. Each of these masses forms a distinct area with a rounded outline and is surrounded by a fibrous zone.

6. On microscopic examination, it is seen that the process is going on chiefly in the capsule and at the periphery of groups of lobules, masses of liver cells being "shaved" off by the invading fibrous tissue.

IN BILIARY CIRRHOSIS—*continued*

siderably diminished in size; the cut surface has a more or less uniform or finely granulated appearance.

6. The single lobules above mentioned are surrounded by bands of fibrous tissue; these bands, however, are not confined to the periphery, but "invade the substance of the lobules."

SYPHILITIC CIRRHOSIS (CONGENITAL) OF THE LIVER

242. This condition is met with in children who come into the world still-born, or who die shortly after birth, with all the marks of syphilis upon them, but sometimes also in children in whom the symptoms of syphilis may be almost absent. In well-marked cases the liver, *on naked-eye examination*, is found to be enlarged; on its surface there are frequently purplish nodular projections; the tissue is firm, tough, and pale, the pallor being more marked at certain points where little pearly white areas are surrounded by a yellow and then by a more vascular zone. These pale areas are about half an inch in diameter, and in them the largest amount of new connective tissue is found. If the disease be very far advanced, the lobules are almost entirely obliterated, and no definite structure remains, the parenchyma appears yellow, mottled with reddish- or greyish-brown, and delicate looking striæ run irregularly through it. It is to be remembered, however, that to the naked eye the structure of the liver may appear to be little altered, even when grave microscopic changes are present; then the only gross evidences of a diseased condition are the increased weight and firmness of the organ. Harden (§§ 59–64), stain (§§ 103 and 158), clear (§ 193), and mount (§ 199).

($\times 50$).—Near the portal spaces, in which is an increase in the amount of fibrous tissue, there may be seen, apparently continuous with the perilobular tissue, a quantity of clear-looking material with numerous rounded nuclei. Between the clear bands are small linear or Y-shaped masses of liver cells; these are separated from one another by spaces, two or three, or even more times the diameter of the deeply stained masses, which are always smaller where the clear spaces are

wider. Further away from the portal spaces the tissue becomes more and more like that seen in a normal liver, and at certain points the structure is that of an almost normal liver.

($\times 300$).—The deeply stained masses are now seen to be rows of

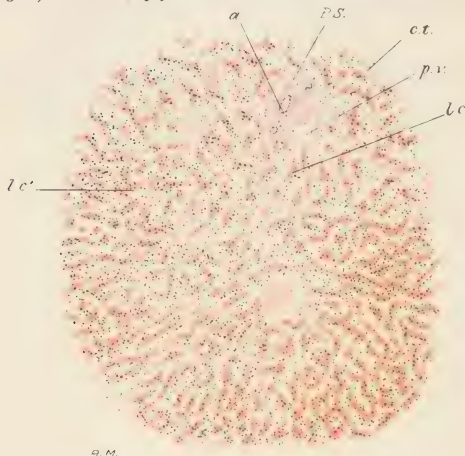


FIG. 53.—Drawing from a section of syphilitic cirrhotic liver. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

P.S. Increase of fibrous tissue in portal spaces. This increase of fibrous tissue is seen to extend from the space for some considerable distance into the lobules, the columns of liver cells (*l.c.*) are more atrophied at the margin than at the centre of the lobule (*l.c'*).

c.t. Nucleated fibrillated tissue between the atrophied liver cells.

a. Bile duct.

p.v. Portal vein.

parenchymatous liver cells undergoing more or less marked changes. Where the rows of liver cells are comparatively broad, the structure of the cell is as yet little altered; there is simply a slight compression of the cell. Where the rows are narrow, there are more extensive changes; the cells are angular, shrunken, and granular looking, and are evidently undergoing atrophic degeneration; the nuclei are obscured, or in certain cases, altogether lost. The substance between these bands of atrophied liver cells consists of a nucleated connective tissue. Around the connective tissue cells, and apparently

formed by them, is a delicate fibrillated periplast, of which the transparent tissue seen under the low power is composed. The enlargement of the organ is due to the great increase in the amount of intralobular connective tissue. In order to understand the nature of this change, it must be remembered that, communicating with the interlobular lymphatics at the margins of the lobules are "minute spaces extending between the liver cells and the capillary blood vessels, and containing numerous branched connective tissue corpuscles." The capillary vessels are lined by an interrupted layer of endothelial cells, which, like the

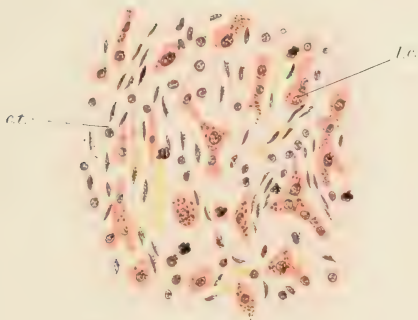


FIG. 54.—Drawing from a section of syphilitic cirrhotic liver. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

l.c. Small masses of granular and somewhat atrophied liver cells, between which is an increased amount of nucleated and fibrillated connective tissue (*c.t.*).

connective tissue corpuscles, are of mesoblastic origin. This form of cirrhosis consists essentially in a proliferation (*a*) of Kupffer's stellate cells, and (*b*) of the connective tissue corpuscles, or endothelial cells, which may be said to line the lymph spaces between the capillaries and the liver cells. Around these proliferated cells a fibrillated collagen is formed; then follow the gradual compression and atrophy of the proper parenchyma of the organ, giving rise to a continually increasing interval between the columns of liver cells, which are thus cut up into short, detached, granular, angular, or linear masses; the vascular supply is greatly altered.

In sections stained by Levaditi's method (§ 158) ($\times 50$) examine the specimen for the above conditions.

($\times 800$).—In the interstitial tissue spirochætes (see § 493), very dark, almost black, in colour, may be seen lying between bundles of connective tissue, the nuclei of which, along with leucocytes, are stained blue, the fibrillar tissue green; the nuclei of the liver cells are also blue and the liver cells themselves of a brownish-green. These liver cells are often degenerated and vacuolated; their nuclei may be broken up, whilst small round cells may be contained in the body of the cell. Within vacuoles in the parenchymatous cells the spirochæte may often be demonstrated following the outline of the wall of a vacuole. These spirochætes may also be seen lying around the liver cells in the bile capillaries and even in the larger ducts, within and around Kupffer's stellate cells which bound the capillary vessels, in the dilated lymphatics, and lying free in the lumina of the blood vessels, especially those of the sublobular veins. In the perivascular connective tissue they appear to be especially numerous, as also in those liver cells in which large quantities of golden-brown granular pigment are deposited. It may be noted that the lymphocytes and the large mononuclear cells are often increased in number and accumulate in small foci near the lymphatics in the connective tissue. Here and there some of the smaller vacuoles may be completely plugged with these spirochætes, which seem to resist putrefactive changes much longer than do the tissues by which they are surrounded.

SYPHILITIC GUMMA OF THE LIVER

243. The syphilitic gumma, closely related to the above form of cirrhosis, is usually described when it has reached the caseous stage; but it should be noted that here caseation is merely a degenerative process taking place in the gumma. In the livers of adults this syphilitic lesion is usually met with in the caseous form only. To find a gumma in process of growth it is necessary to examine the liver of a syphilitic child, in which they are frequently found in connection with the syphilitic form of cirrhosis. Such a growing gumma is a tumour, varying in size (from the size of a pea to that of a marble, or even larger), of a rosy-grey colour when seen on section, and *containing vessels*; the "growth" gradually merges into the surrounding tissues with which it is intimately connected. This surrounding tissue is made

up of very vascular fibro-cellular bands. On the surface of the liver are irregular patches, deep red in colour (redder than the rest of the liver substance).

The caseous gumma is usually met with in the adult, situated near the surface of the liver; this caseous mass is usually surrounded by a fibrous capsule, from which long radiating processes shoot into the neighbouring parenchymatous substance of the liver. It is usually met with on the upper surface of the organ, and most frequently near the suspensory ligament. In consequence of the contraction of the fibrous capsule surrounding the mass, there is a distinct depression at the periphery; and the caseous nodules appear to be contained within fibrous cicatrices situated near the surface of the liver. The liver tissue is usually brown or bile-stained, and is evidently undergoing atrophic changes. Harden (§§ 58-64), stain (§§ 102 or 103, 110, 126, 158, 162, and 164), and mount (§ 195 or 199).

($\times 50$).—On examining a section of a nodule taken from the liver of a syphilitic child, it is seen that the growth is situated in newly formed intralobular fibrous tissue; in other words, the formation of a gumma is preceded by a syphilitic cirrhosis identical with that already described. At certain points the development of fibrous tissue has taken place to such an extent that there are numbers of strongly marked fibrous bands intersecting the lobules and cutting up the liver tissue. These fibrous bands are highly vascular, vessels in all stages of development being seen in their substance. In the fibrous band and around the vessels the developing gumma is seen in the form of a number of deeply stained embryonic cells, an area which gradually increases in diameter; as this extends peripherally, the cells near the centre become angular, granular, atrophied, and (when stained with picro-carmin) yellow.

At this stage the gumma is an actively growing mass of connective tissue, for it may be observed that around the embryonic cells at the periphery is a delicate fibrillated stroma. Whilst the growth is going on in the gumma, certain changes are also to be observed in the vessels in the immediate neighbourhood. If a vessel be examined in transverse section, it will be seen that its walls are thickened, and that the increase in thickness takes place, principally, in the "intima," or within the internal elastic lamina (which in the hæmatein and van Gieson stained specimen is bright yellow). In some cases this thickening of the "intima" is so great that the lumen of the vessel

is almost obliterated; and it is to be noted that even where the obliteration is not complete there is, frequently, a coagulum fixed in the lumen, which might prevent the passage of blood through the vessel.

($\times 300$).—(1) The granular shrivelled cells in the centre of the mass are readily made out; they are small in size, are closely packed together, and are frequently stained yellow, even before caseation has actually set in. (2) Surrounding these central atrophied cells is a zone of larger embryonic cells, or of endothelioid and fibroblast cells, very similar to those met with in tubercle; they are of various shapes and sizes, and many of the endothelioid cells contain several nuclei. (3) Between these endothelioid cells, or surrounding them, and the fibroblasts, is a fibrillar periplast. (4) External to this zone are numerous small round cells (polymorpho-nuclear leucocytes) or their nuclei, which, as in the case of the nuclei of the endothelioid cells, take on the carmine or logwood stain very readily. Mononuclear cells, large and small, may also be made out. In the vessel, with the outer wall of which the gummatous growth is practically continuous, the endothelial cells of the "intima" have undergone enormous proliferation, and the flattened cells are so arranged layer upon layer, that they may almost block the lumen of the vessel. Within the narrowed tube a coagulum of fibrin is frequently found, with a few white blood corpuscles at the periphery of the clot, adhering to the wall. It is highly probable that the caseation which almost invariably ensues in gummata is brought about (1) by the specific action of the syphilitic virus (*Spirochaeta pallida*, which should be searched for especially in young and actively growing gummata, as in the syphilitic liver above described) on the tissue elements; (2) by the contraction of the tissue at the periphery of the gumma itself and of the fibrous tissue surrounding it; (3) by the *endarteritis obliterans* (see § 266) causing the obstruction of the vessels either alone or (4) in conjunction with a coagulum which forms on its roughened and inflamed walls. The change in the artery may take place at some point outside the gumma, but so long as the blood supply to the gumma is cut off, the effect is the same—fatty degeneration of the tissues, followed, first, by caseation, and later, by absorption and cicatrization. The section of the gumma is then hard and firm, and cuts almost like gritty india-rubber.

Where caseation has taken place, as in the gummata found in the

adult, harden (§§ 60-64), stain (§§ 102, 103, or 104, 117, 135, 158, and 162), and mount (§§ 195 or 193 and 199).

($\times 50$).—The centre of the mass is stained yellow, the caseous



FIG. 55. Drawing from a section of liver with hepatitis gummosa. Stained with alum hæmatein and van Gieson's stain. ($\times 20$.)

- f.t.* Continuation of the fibrous tissue from the capsule around the caseous mass into the substance of the liver, in which are numerous sections of embryonic vessels (*v.e.*).
- l.c.* Small patches of liver tissue left between the bands of fibrous tissue.
- C.G.* Fibrous external zone; and *Cas. g.* caseating central zone of softening gumma just below the capsule.

material taking on the picric acid stain, but none of the carmine. Around the caseous portion is a distinctly fibrous zone, by the contraction of which the indentation of the capsule of the liver at the outer

margin of the growth is brought about. The fibrous capsule gradually shades off and sends out long radiating processes into the surrounding cirrhotic tissue, between the bands of which may be seen the Y-shaped trabeculae of atrophied liver cells similar to those seen in syphilitic cirrhosis. The "adventitia" of the vessels in the neighbourhood is considerably thickened, whilst the proliferation of the endothelium lining the vessel is also well marked.

($\times 300$).—The caseous yellow mass is made up of shrivelled granular débris, into which run bands of fibrous tissue, apparently continued from the capsule of the gumma. Crystals of cholesterin and of stearic acid are met with, as well as fat granules, or even globules—readily recognised with the aid of osmic acid staining. In the fibrous capsule are a number of lymph spaces which contain blackened globules, these in all probability having been carried from the caseous mass. In this way the gumma may be gradually absorbed, the surrounding fibrous tissue being exceedingly vascular and well supplied with lymphatics. Under this power the changes already described as seen in the neighbouring vessels may again be noted, as may also those described as being identical with the changes met with in syphilitic cirrhosis.

The middle coat may undergo the lardaceous or waxy degenerative change, a degeneration so common in syphilis in its various forms.

It is difficult to look upon the whole process as anything more than a caseation of parts or areas of newly formed fibro-cellular tissue, brought about by the action of the specific virus, and, as pointed out by Friedländer, Heubner, and Greenfield, by the cutting off of the blood supply as a result of *endarteritis obliterans*.

SYPHILITIC CICATRICES

244. Syphilitic cicatrices appear to result from the two previous lesions. The liver may be cut up into a series of small masses by bands of fibrous tissue. These bands run in from the thickened Glisson's capsule, the thickening being due to perihepatitis, or inflammation of the capsule, as a result of which the liver becomes firmly adherent to the diaphragm. If a section be made through one of these fibrous bands, numbers of small gummata may often be found scattered through it. Harden (§§ 60–63), cut (§ 82 *et seq.*), stain (§ 102, 103, or 104, 158, 162), and mount (§ 195 or 199).

($\times 20$).—The cirrhosis is seen to begin at the surface—in the capsule—from which bands of pink fibrous tissue run, irregularly, through the organ. Between these fibrous bands, especially near the margins of the mass of fibrous tissue, are thin rows of atrophied liver cells similar to those seen around gummata, and in the syphilitic cirrhotic liver. All this should be verified ($\times 300$).

ACUTE OR SUBACUTE YELLOW ATROPHY

245. In the stage at which, in acute or subacute yellow atrophy, the liver comes under examination, the organ is usually considerably diminished in size; the capsule is markedly wrinkled, and may be caught up between the fingers. The tissue is soft and flabby, in some cases almost of fluid consistence; the surface is mottled, yellow ochre with dark red patches. On section the colour and appearances are much the same, and, as a rule, all traces of the individual lobules are lost, though there may be a patch, here and there, in which the centres of the lobules are red, the outer zones being yellow or greyish-yellow. Under the capsule, in addition to the larger red or brownish-red patches, irregular in outline, varying in size, often appearing almost like infarcts or blood clots, are small punctiform hæmorrhages similar to those found on other serous surfaces in this condition.

On examining scrapings from the cut section ($\times 300$) a number of liver cells in various stages of degeneration and atrophy are observed. They are almost invariably bile-stained and extremely granular; the nucleus is obscured, and in the cytoplasm are found numerous small granules of pigment. Along with these cells are a number of red and white blood corpuscles, and often crystals of leucin, tyrosin, and xanthin. (These may be seen in the blood and urine of the patient during life, where their presence appears to be due to imperfect oxidation of the proteid substances—they are incomplete oxidation products.)

Harden (§ 56 or 63), stain (§ 106 or 150), and mount (§ 195 or 199).

($\times 80$).—In the portal spaces, especially around the vein, a number of round cells with deeply stained nuclei are to be seen. We have, in fact, evidence of an interstitial inflammation, an interlobular exudation. From the interlobular spaces and fissures the process extends into the lobules between the columns of liver cells. The parenchymatous cells are shrunken and angular, are stained orange-

yellow, and appear to be very irregularly arranged; frequently they

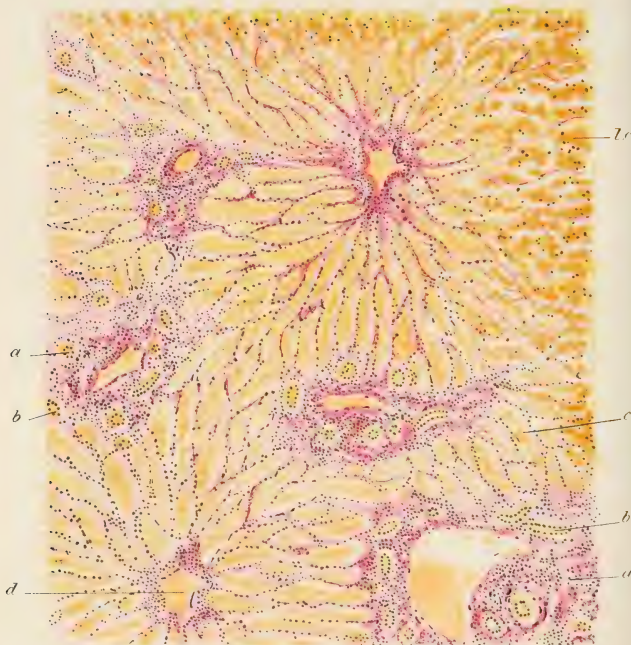


FIG. 56.—Acute yellow atrophy of the liver, section stained with alum hæmatein and van Gieson's stain. ($\times 80$.)

- a.a.* Interlobular spaces in which is a considerable amount of small-celled infiltration and some cedematous swelling of the connective tissue fibrils. In this the bile ducts (*b.*) appear to be increased in number.
- c.* Portal capillaries containing much blood, a few round cells between, but the liver cells have almost disappeared.
- d.* Hepatic venule surrounded by swollen fibrillar tissue. A number of nuclei of small round cells are also seen.
- l.c.* Liver cells, many of them atrophied and shrivelled, especially at the margin of the mass, between the red and the yellow areas. Some of the cells contain granules of dark brown pigment.

have disappeared from the centre of a lobule or from several lobules.

In the hæmorrhagic patches the tissue may be completely disorganised.

($\times 300$).—In the newly formed tissue, made up of polymorphonuclear leucocytes, lymphocytes, and large mononuclear cells, a number of small bile ducts may be recognised as elongated double rows of nuclei; some of these are pre-existing bile ducts, enlarged, whilst others appear to be of entirely new formation. The liver cells are shrunk and the protoplasm is atrophied, so that the outlines are irregular; they are of a yellow colour, even when they contain no brown pigment. Many of these, however, contain much granular pigment, as noted in the examination of the scrapings. In the subacute form there may be evidence of the formation of new liver cells. In a fresh section, in addition to the above appearances, the crystals of leucin and tyrosin are readily distinguishable. In the early stages of the disease micrococci of considerable size have been demonstrated¹ lying “in the portal canals, filling the arteries, and in the peripheric part of the lobule between the liver cells, filling up apparently the capillaries between them” (Dreschfeld).

TUBERCLE OF THE LIVER

246. The liver is one of the best organs in the body in which to study the structure and development of tubercle; the growth being uncomplicated by catarrhal changes, such as occur in the lung, the formation of new tissue, and subsequent degeneration and fibroid changes may be followed very easily.

Tubercle nodules in the liver are seen first as small translucent grey, or opaque yellowish, or green granulations, either in the capsule itself, or near the surface of the organ. It is only in the very earliest stages that these tubercle masses are grey; when the growth has become fully developed, it is no longer vascular, and rapidly becomes softened, cheesy looking, and bile-stained. Harden a section of the liver containing one of these small grey granulations (§ 58 or 63), stain and mount (§§ 102 and 195, or 104 and 199).

($\times 50$).—In an interlobular space, or just at the margin of a lobule, may be seen a granular-looking mass pushing aside the liver cells, and apparently gradually infiltrating the surrounding tissues. This mass, the tubercle follicle, is usually deeply stained, but towards

¹ A case of acute atrophy of liver.—*Lancet*, 1884, i. p. 606.

the centre is a more deeply stained ring, about the size of a small pin's head, which surrounds a lighter centre—a giant cell.

($\times 300$).—The elements of which the tubercle follicle is composed are well seen. (1) At the periphery of the growth, and spreading in between the liver cells, which are pushed aside and gradually atrophy, are numerous small round cells; these take on the nuclear stain, and appear to be little more than the nuclei of young connective tissue cells with some lymphocytes and polymorpho-nuclear leucocytes. (2) Nearer



FIG. 57.—Acute miliary tubercle of liver. Stained with alum hæmatein and van Gieson's stain. ($\times 40$.)

- a.* Central hepatic vein.
- b.* Portal canal.
- c.* Giant cell tubercle follicle at margin of lobule.
- d.* Tubercle follicle without giant cell.
- l.c.* Liver cells in columns between portal capillaries.

the centre, or rather running amongst the inner layers of these small cells, is a network of fibrous tissue, stained pink; in some cases, especially where the nodule is still young, there is very little of this fibrous tissue. (3) As the centre is neared, the tissue opens out into a network with wider spaces, in the meshes of which are found larger cells of various shapes. Many of them contain two, three, or even more nuclei. These latter appear to be endothelioid cells, such as are found lying on all bundles of connective tissue, especially where

growth is rapid. (4) The centre of the tubercle is occupied by the giant cell, which is seen as a large branching cell, from the periphery of

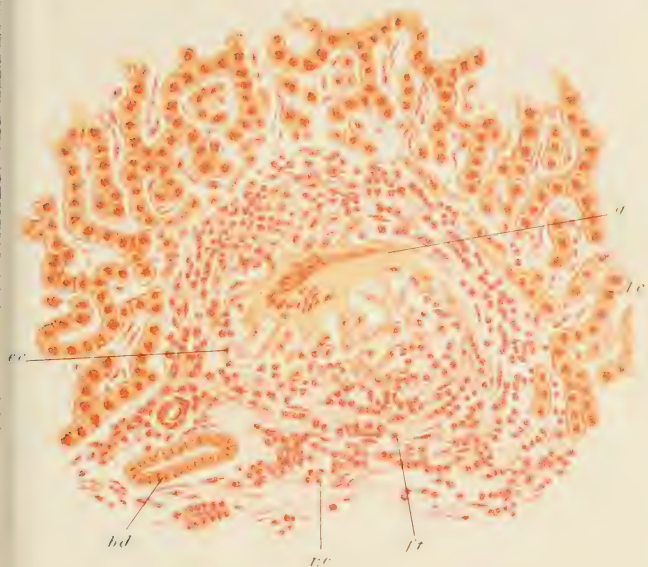


FIG. 58.—Drawing from section of tubercle of the liver. Stained with picro-carmin. ($\times 300$.)

- g.* Giant cell, with nuclei at the periphery, and sending off branching processes.
- e.e.* Endothelioid cells, lying on fibrillæ of the network of connective tissue, with which the branching processes of the giant cell appear to anastomose.
- r.c.* Round cells, young connective tissue corpuscles, and leucocytes appearing towards the periphery of the mass.
- f.t.* Fibrous tissue, forming a kind of capsule to the tubercle. In this capsule are a number of rounded nuclei.
- l.c.* Columns of liver cells, those near the tubercle somewhat flattened and atrophied; between them are rounded nuclei, etc., extending from the growing tubercle mass.
- b.d.* Small bile duct. *a.* Branch of hepatic artery.

which processes run to join the fibrous reticulum; in the liver these processes can often be very distinctly seen. (5) At the periphery of the giant cell are numerous rounded, deeply stained nuclei, each about

the size of one of the small cells found at the periphery of the tubercle, but they appear to be somewhat more deeply stained. They form a distinct belt or zone around the cell, as a single or double row, and they bound the bright canary yellow area, which occupies the body of the cell, and is, as a rule, perfectly homogeneous and translucent. In this there may be one or more clear spaces or vacuoles.

The tubercle follicles (giant cell systems, as they are called), are developed in or near the interlobular or portal spaces. Around the primary follicle numerous other follicles may be formed; these being non-vascular cut off the supply of nutriment from the central part, which rapidly undergoes caseous degeneration and dies. The small bile ducts are involved in the caseous mass, into which bile is poured, with the result that tubercle in the liver, except in the very earliest stages, is invariably of a greenish-yellow colour (all dead matter in the liver becoming bile-stained).

These tuberculous areas may gradually enlarge until they form a yellowish-green mass of considerable size, the centre of which undergoes caseation and softening, forming a large cyst with fibrous or gelatinous-looking walls. In the gelatinous-looking wall are found numerous tubercle follicles. Contained within the fibrous capsule is a green, soft, putty-like mass, composed of granular *débris*, fatty globules, and shrivelled, angular, and atrophied cells. Sometimes the caseous material is replaced by a clear watery fluid—bile from which the bile acids, pigments, and salts have been absorbed. The dense lymphatic system around the bile ducts may account for the special affection of these ducts by tubercle.

In one form of tubercle the walls of the larger bile ducts are specially affected, tubercle follicles being found in the submucous layer; these follicles rapidly caseate, and ulceration ensues as the blood supply to the epithelium is cut off by the non-vascular tubercular growth beneath. The process extends along the lymphatics, but it also spreads by direct infection, by application of the specific infective tuberculous material to the opposite wall of the duct or to the surface at some distance. This form of tubercle should be studied along with tubercular ulceration of the intestine and tubercular pyelonephritis, both of which, in many respects, it resembles very closely. Frequently other conditions, such as cirrhosis—which is especially met with in the livers of tuberculous children—waxy changes

in the vessels, fatty infiltration or degeneration with atrophy and shrivelling of the liver cells, are found associated with tubercle of the liver; in examining a tubercular liver these complications should be borne in mind, and such changes carefully searched for and noted.

LIVER FROM A CASE OF LEPROSY

247. This liver was flabby and somewhat pale, the number of grey areas being seen especially around the portal canals, the outlines of the lobules were fairly well marked, evidently the result of some fatty infiltration. Fix and harden (§ 58 or 63), cut (§ 94), stain and mount (§§ 183, 193, and 199).

($\times 50$).—At the periphery of each lobule there is distinct fatty infiltration. In the portal spaces, which are rather more prominent than usual, there is proliferation of the connective tissue and endothelial cells, whilst there seems also to be a slight increase in the number of leucocytes and some swelling of the connective tissue fibrils. The endothelium between the columns of liver cells is more marked than usual, the cells apparently being considerably swollen, and in some of them even under this power, collections of what appear to be small red granules may be made out very distinctly. Near certain of the portal fissures many of the liver cells are very much atrophied and broken down. Here also there is considerable increase of the endothelial and connective tissue cells, which, however, like the liver cells, have their outlines obscured. In this tissue little areas containing deeply stained granules, single or in groups, are very evident.

($\times 1000$).—Confirm the above. The little groups of granules are now seen to be collections of deeply stained rod-shaped organisms very similar to the tubercle bacilli, but having a very definite distribution. In certain of the swollen endothelial cells (Kupffer's stellate cells) lying between the columns of liver cells, often almost filling the cell and lying close to the nucleus, are single bacilli or groups of bacilli. Where these groups of bacilli are large the cell may be disintegrating and the nucleus badly stained, but where there are single bacilli only the outlines of the cell and the nucleus are still prominent. In the pale degenerating area seen under the low power the leprosy bacilli are very numerous, and in some cases appear to be actually within the liver cells, in this case both bacilli and liver cells are breaking down and becoming granular, though the differential staining is fairly well

marked, as the nucleus still reacts to the methylene-blue in a characteristic, though feeble, fashion. This condition differs from tubercle in that no specific tubercular nodules, the result of proliferative activity of the connective tissue, can be made out. Here the proliferation is

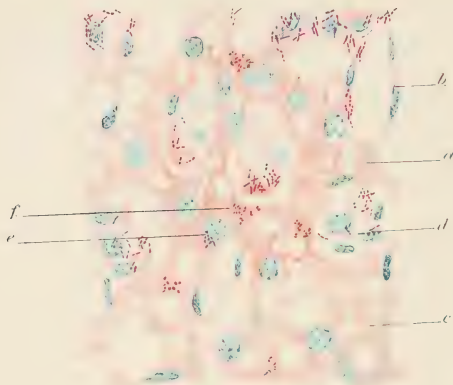


FIG. 59.—Section of the liver from a case of leprosy. Stained by the Ziehl-Neelsen method; decolorised with 5 per cent. sulphuric acid.

- a. Protoplasm of liver cell.
- b. Endothelial cell with elongated nucleus; at one extremity of this nucleus are leprosy bacilli contained within the cytoplasm. These correspond to the Kupfer's stellate cells.
- c. Fat globule in liver cell.
- d. Endothelial cell with well-formed bacilli near nucleus.
- e. Leprosy bacilli free and around nucleus of a liver cell.
- f. Group of degenerating bacilli in hepatic cell.

far more diffuse and associated with a granular degeneration of both liver cells and connective tissue resulting from the destructive activity of the numerous leprosy bacilli contained within their protoplasm.

LYMPHADENOMA OF THE LIVER

(*Hodgkin's Disease*)

248. In Hodgkin's disease the organ is enlarged, smooth, and pale (Goodhart in "New Sydenham Society Atlas"); in it are seen small,

pale pink or grey nodules, which specially affect the portal canal, spreading thence into the lobules. They may be numerous or few in number. Sometimes these nodules are larger, when they assume a "greyish-yellow colour," and are tough, but in some cases they are undergoing caseation and softening. Each of these masses, varying in size from a pin's head to a small marble, is surrounded by a zone of reddened tissue, which appears to be made up of dilated venous capillaries. There is a different form, or a more advanced stage, where grey streaks appear not only on the surface under the capsule but also throughout a section. This condition of the liver is almost invariably associated with a similar condition of other organs—spleen, kidney, etc. etc., with induration and enlargement of the lymphatic glands, first those of the neck, then those of the axilla, and so on throughout the body. Harden (§ 62 or 63), cut (§ 94 *et seq.*), stain (§§ 102 or 103 and 160 and 162). The growth appears to begin in the portal spaces, and gradually extends into the substance of the lobule running from the periphery towards the centre, apparently along the walls of the capillaries, the endothelial cells of which become increased in size, and are often multinucleated; it consists of a network of fibrous tissue packed with leucocytes, lymphoid cells, hyaline cells, and endothelioid plates; at the margin of the growth the liver cells are atrophied and angular, their nuclei are obscured, and the protoplasm of the cell appears to be converted into fatty granules. In some of the cells there is an appearance of vacuolation—probably due to the presence of fat globules.

LEUCOCYTHÆMIA OR LEUKÆMIA OF THE LIVER

249. The liver is usually enlarged, in some cases markedly so, and is firm and fleshy to the touch; the surface is smooth and pale. Small subserous hæmorrhages are often seen, but these are lighter red than usual. On section we have the same pale smooth surface; between the lobules, in the interlobular fissures and spaces, the pallor is more distinctly marked, and we have a network of irregular pearly white veining, the tissue enclosed in the meshes of which is more or less fatty or anæmic looking; the margin of the lobule appears to project beyond the general surface of the section.

Harden (§ 60, 62, or 63), stain (§ 102 or 109), and mount (§ 195 or 199).

($\times 50$).—In the interlobular spaces and fissures are enormous collections of deeply stained nuclei of cells (leucocytes and myelocytes), by which the lobules are very distinctly outlined. Masses of these cells are also seen between the parenchymatous cells in the peripheral zone of the lobule, in the spaces and tissues surrounding the vessels; the intercolumnar capillaries themselves are crowded with them. In advanced cases the whole lobule may be infiltrated, and small hæmorrhagic masses, in which are large numbers of leucocytes, are

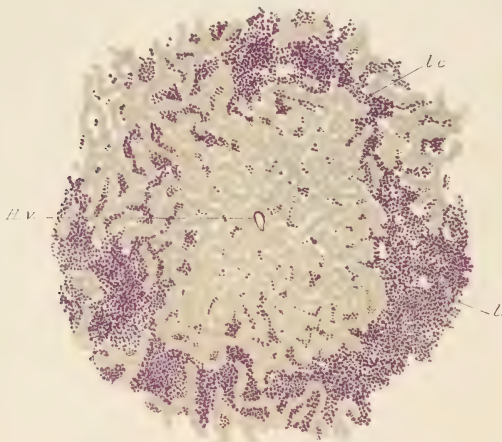


FIG. 60.—Section of leucocythæmic liver. Stained with logwood.
($\times 70$.)

H.v. Central or hepatic vein.

l. Leucocytes, especially numerous at the periphery of the lobule.

l.c. Rows of liver cells between the capillary vessels.

scattered at irregular intervals throughout the liver substance, but especially under the capsule.

($\times 450$).—The infiltration around the vessels is readily made out; the capillaries are crowded, both inside and out, with the deeply stained cells, so that in many places the liver cells appear to be atrophied, and even destroyed, by the pressure of the myelocytes, though otherwise they may remain unchanged.

These small cells, when carefully examined, are in all respects

like the so-called wandering cells, though in many cases the nucleus has assumed a solid instead of a lobed or polymorphous form, and are surrounded by no stroma of any kind, though a few delicate threads of *coagulated fibrin* may sometimes be seen lying in the normal connective tissue spaces of the part; in this respect leucocythæmia differs very markedly from lymphadenoma, in which condition a distinct stroma or

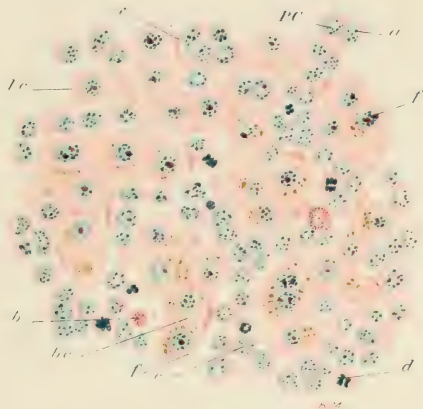


FIG. 61.—Section of liver from case of myelogenous leukaemia.
Stained with eosin and methylene-blue. ($\times 500$.)

- P.C. Portal capillaries, containing
- a. Myelocytes, neutrophile;
 - b. Myelocytes, eosinophile;
 - c. Leucocytes, polymorpho-nuclear;
 - d. Hyaline cells with mitotic figures;
 - e. Endothelial cell lining capillary.
 - f. Liver cells containing altered blood pigment.
- L.C. Normal liver cells and
- b.c. Bile canaliculus between adjacent liver cells.

network of *fibrous tissue*, containing small round, and larger endothelioid, cells is seen.

In many cases of leucocythæmia, pigmentation of the liver cells in the peripheral half of the lobule is a characteristic feature. It is similar to the condition that has been observed in the liver in pernicious anæmia.

The pigment differs somewhat from that met with in chronic

venous congestion. It is essentially an iron pigment, for when a section is soaked for a few minutes in a weak solution of ferrocyanide of iron, and then washed in water, to which a few drops of hydrochloric

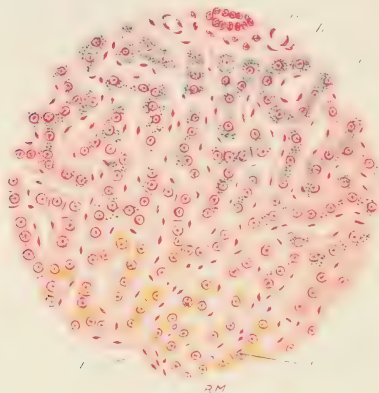


FIG. 62.—Section of liver from a case of pernicious anæmia. Stained with alum carmine after the Prussian-blue reaction has been obtained. ($\times 300$.)

- a.* Portal canal containing connective tissue.
- b.* Bile capillary, and *b'*, small branch of hepatic artery.
- c.* Liver cell with deeply stained nucleus and Prussian-blue pigment.
- d.* Hepatic or central vein with distinct wall.
- e.* Pigment, which does not give iron reaction, surrounding liver cells.
- f.* Portal capillaries.

acid have been added, the yellow or golden-brown colour is replaced by a beautiful transparent blue.

TYPHOID LESION

250. There is a condition of the liver induced in prolonged cases of typhoid fever of severe type, which is, probably, common to this and to other diseases. It appears to be a peculiar inflammatory change due to the impaction of some bacterial thrombus in the capillaries of the intermediate zone of the lobule. In addition to the general cloudy swelling of the liver cells, common in febrile conditions, we find scattered throughout the substance of the liver a number of small

yellow or grey specks, each about the size of a pin's head, situated in the above-mentioned position, or in some cases involving the whole of the lobule. Harden (§ 56, 60, or 63), stain and mount (§§ 102 and 195 or 104 and 199).

($\times 50$).—Note that parts of some of the lobules are more deeply stained than is the surrounding parenchymatous tissue. These deeply stained patches are not met with in every lobule, but only here and there, one or two comparatively normal lobules intervening between the affected areas.

($\times 300$).—One of two conditions may usually be observed in the deeply stained portions. In the early stage there is extreme cloudy swelling of the parenchymatous cells, which are so swollen and pressed against one another that their outlines cannot be readily made out. The protoplasm of the cells is very granular and somewhat opaque, so that the nucleus is frequently partially obscured, or even lost sight of. The cloudy swelling is more or less marked in the cells of the whole of the lobule, but is most characteristic in the situations mentioned. In the later stages both protoplasm and nuclei of the liver cells appear to undergo complete disorganisation, until in the intermediate zone of each lobule only a mass of granular débris is to be seen. This mass takes on the pink staining somewhat distinctly, unless it has undergone marked degeneration before the death of the patient, in which case it takes on a more yellow stain (with picro-carmin), as do all necrosed tissues (it is bile-stained when seen *en masse* with the naked eye). This condition appears to be similar to that met with in some cases of dysentery, where the formation of abscesses in the liver is commencing.

ABSCESSES OF THE LIVER

251. (1) *Tropical amœbic abscess*.—This form of local necrosis or suppuration of the liver is usually met with in hot climates, and appears to be associated with antecedent dysenteric disease of the bowel, especially when amœbic organisms are found in the fæces or in the dysenteric lesions of the intestine. It usually occurs as a single abscess, sometimes there are two or three; they are rarely numerous, though even very numerous minute abscesses may be found near the surface or scattered throughout the substance of the organ, deeply situated in the right lobe of the liver. When such an abscess is opened it is found to contain a creamy, purulent material, tinged pink by the presence

of a small quantity of blood: this pus-like material is viscid or slimy, and has a peculiar characteristic sickly odour, but is not putrid.

($\times 300$).—On examination of the fluid discharged from the abscess in a neutral solution ($\frac{3}{4}$ per cent. salt, § 36, 5) a considerable amount of granular débris, fragments of chromatin, pigment granules, and a few red blood corpuscles may be found, but one is struck by the comparatively small number of pus corpuscles present. The débris consists of liver cells in various stages of disintegration, and delicate shreds of connective tissue. The pus from an amœbic abscess should be kept in a clean glass vessel at 80° C., and should be examined as soon as possible. Fix film preparations (§ 171), harden (§ 58, 61, or 63), stain (§§ 110, 115, 117, 126, and 148), and mount (§§ 193 and 199).

($\times 800$ or 1000).—No organisms of any kind are, as a rule, to be found in this pus-like mass when the abscess is first opened, but after the discharge has continued to flow for a short time, especially if it remains alkaline, well-defined amœbæ (*Amœba dysenteriae*, *Entamœba histolytica* of Schaudinn) may be demonstrated. These amœbæ are usually from 24 to $30\ \mu$ in diameter, though they may be as small as 10 or as large as $40\ \mu$. They usually disappear when the fluid becomes acid (Marshall). They are globular, ovoid, or pear-shaped, and consist of a well defined capsule or ectoplasm, which is usually highly refractile and easily distinguishable, and a granular entoplasm in which a series of vacuoles may be seen, whilst in addition there is usually a deeply stained eccentrically placed contractile vesicle or nucleus with a more deeply staining nucleolus. In the small vacuoles a deeply stained point may sometimes be seen; these vacuoles may be extruded through the ectoplasm. In certain cases, red blood corpuscles and even bacteria may be seen lying in the substance of these amœbæ.

These organisms are described as occurring in an active or amœboid stage and in a cystic or resting stage. During the amœboid stage, if examined in a warm chamber, they are seen to exhibit active movements. The ectoplasm is not so readily distinguished as during the resting stage. The organism throws out, often very quickly, blunt pseudopodia which are retracted almost as quickly, sometimes taking in with them red blood corpuscles, bacteria, etc. These pseudopodia are not readily separated from the body of the organism.

If these amœbæ can be kept under observation for some time evidence of amitotic division may sometimes be seen. It is difficult,

however, to follow this except by examining a number of organisms at different stages, as the amœba soon loses its vitality and rapidly undergoes disintegration. For a description of the cystic stage, see § 365.

In the liver, in the neighbourhood of the abscess, and in the walls of the abscess itself, the zone of the portal capillaries is, as a rule, somewhat deeper in colour than the zone of the hepatic vein. The walls of the abscess are ragged, and shreds of liver tissue hang

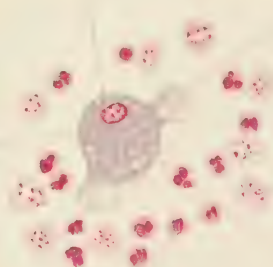


FIG. 63.—Pus from hepatic abscess in a case of tropical dysentery, *Entamoeba histolytica* (amœboid stage). Stained by Benda's method. ($\times 1000$ diam.)

- a. Vacuolated protoplasm of amœbæ.
- b. Blunt, tough pseudopodium.
- c. Nuclear vesicle.
- d. Small mononuclear cell (lymphocyte).
- e. Polymorpho-nuclear pus cell.
- f. Large mononuclear pus cell. ? Mast cell.

into the abscess cavity. This inner portion of the wall has a peculiar mucoid, sloughy appearance, whilst beneath it the tissue is somewhat firmer and more vascular.

Fix and harden small pieces of the liver and abscess wall (§ 58, 61, 63, or 135), embed and cut (§ 94), stain (§§ 102, 110 (*b*), 115, 126, and 148), and mount (§§ 193 and 199).

($\times 50$).—The portal capillaries are congested and are full of blood containing an increased proportion of leucocytes. The wall

of the abscess consists of necrotic tissue in which, even under this power, amœbæ may be fairly easily distinguished. The necrosis, however, extends for a considerable distance beyond the zone in which the amœbæ occur, disintegration being determined, apparently, by the chemical products of the amœbæ.

($\times 300$).—A little distance from the abscess the endothelial cells lining the distended portal capillaries are usually swollen. The liver cells are undergoing cloudy swelling and early fatty degeneration. Nearer the abscess and in the distinctly necrosed area the swollen endothelial cells are detached from the wall. Some of these cells contain a considerable quantity of yellow pigment, which, however, does not give any Prussian-blue reaction. The liver cells, fatty and disintegrated, have imperfectly stained nuclei. The amœbæ in the necrosed area, and in what Marshall calls the reticular area outside this, are like those met with in the pus, or they may be in what has been described as the resting stage. Marshall points out that the amœbæ probably reach the liver by the portal circulation from the dysenteric lesions in which amœbæ are found; in the large intestine he was certainly able to demonstrate the presence of these amœbæ in the thrombi in the small branches of the portal vein; he also found them lying free in the tissues and in the lymph spaces. Other observers maintain that the amœbæ may pass through the walls of the intestine, through the peritoneal cavity, and so on to the liver, where they give rise to typical abscesses. They may be found near the convex surface under the diaphragm, or near the concave surface above the bowel. Although no bacteria are to be found in many cases of amœbic abscess, in certain cases the amœbæ may be accompanied by the *Bacillus coli communis* and the pus-producing streptococci and staphylococci. This bacterial infection, however, appears to be a process quite secondary to the true amœbic infection.

(2) *Pyæmic abscess*.—This form of abscess is comparatively rare in the liver, unless there is some source of putrefactive infection in the tract from which the portal blood comes—such as a putrid ulcer of the mucous surface of the stomach or intestinal canal, or septic disease of the pelvic organs, uterus, rectum, etc.; it may be caused by phlebitis, associated with the presence of a calculus in the portal vein. In all these conditions there is absorption of some septic material from the primary infecting source by the portal vein. It is said that in injuries to the cranial bones, where there is suppuration extending to

the open veins of the *diplœe*, there is a tendency to the formation of pyæmic abscess in the liver, but this has been denied by authors who have examined numerous cases of this form of disease and of injury of the cranial bones.

Such abscesses are usually small and multiple, and are more or less wedge-shaped. They appear to be limited to certain branches of the portal vein, and are found especially near the surface of the organ. On opening into one of these abscesses a quantity of very

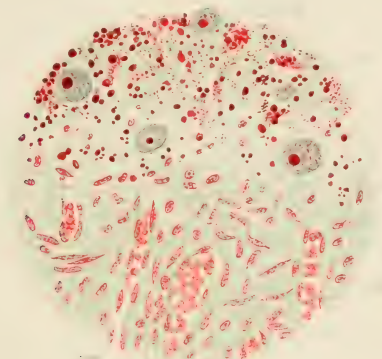


FIG. 64.—Edge of abscess wall in the liver, from a case of tropical amœbic dysentery. Stained by Benda's method. ($\times 300$.)

- a.* Necrosed area in which amœbæ (*b.*) and granular débris are well seen.
- c.* Chromatin granules in zone between necrotic area and Marshall's reticular area, *e.*
- d.* Congested vessels with swollen endothelial cells.

foul smelling, ashen-grey or greenish pus is evacuated: this is found to be made up of ordinary pus corpuscles and shreds of tissue in the last stages of disintegration. The walls of the abscesses are sloughy and ragged looking, and are sodden and infiltrated with serum and pus; surrounding this sloughy and sodden zone is an area or zone which appears to be highly injected and vascular.

These abscesses are probably the result of septic inflammatory changes in the corresponding branches of the portal vein, in which septic thrombi are frequently found. Harden a piece of the liver

near the abscess with a part of the wall (§ 56, 58, 61, or 63), and stain and mount (§§ 102, 104, 117, and 199).

($\times 50$).—Around the vessels in this position are numerous polymorpho-nuclear leucocytes stained pink with picro-carmin, blue with logwood, or violet with gentian- or methylanilin-violet.

($\times 450$).—In the section stained in methylanilin-violet look for micrococci, which, when present, are seen as violet stained granular masses, in some cases forming a considerable part of the “clot” in the vessel. In the neighbourhood of these septic thrombi the liver cells are usually granular, or, it may be, completely broken down; the nuclei are also lost, or take on the stain very feebly. In the portal spaces the appearances are similar to those already described as occurring in acute fevers (§§ 240 and 249); in fact, the whole condition resembles, very closely, that described under the heading of “typhoid lesions.”

In both of the above abscesses, whether in the single or in the multiple form, it is to be noted that the walls are “sloughy,” and that there are ragged shreds of tissue projecting into the abscess cavity. This is an important diagnostic feature, for in the next form of abscess it will be found that the walls are usually smooth and well defined.

(3) *Suppuration in the hydatid cyst of the liver.*—Where suppuration takes place in a hydatid cyst as a result of direct violence, or from any other cause, the hydatid membrane becomes swollen, and may be entirely broken down and evacuated, but even then the false fibrous capsule formed by the condensed tissue of the organ remains for a considerable time, and bounds the cavity as a smooth, well-defined wall; hooklets (§ 484) by which this condition may be distinguished from either of the above forms of abscess are usually to be found in the discharge.

(4) *Actinomycotic abscesses of the liver* may occur as multiple abscesses sometimes arranged around a large central focus of suppuration. Around the central purulent mass is a gelatinous, pale or reddish tissue in which points of greenish-yellow suppuration may be seen. These small abscesses gradually run together and form peculiar sinus-like abscesses, giving a honeycombed appearance to the tissue; this is seen specially well at the spreading margin of the abscess. At this margin there is evidence of a chronic inflammatory condition gradually invading the surrounding tissue, the central part

breaking down and becoming purulent. In the greenish-yellow pus, yellow, brownish-green, or red granules may be seen, which though somewhat tenacious in consistence are comparatively soft, and may be spread out on pressure between two cover-glasses. These, on microscopical examination, are found to be little masses of the ray fungus (§ 502). Stain (§§ 115, 125, and 502) and mount (§ 199).

($\times 50$).—Throughout the liver, usually near the portal spaces, are

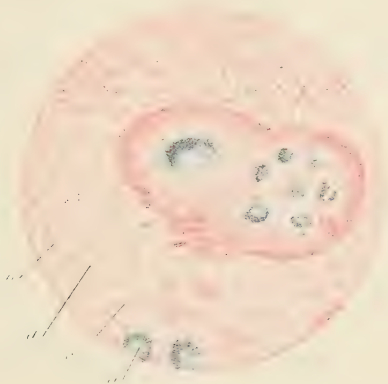


FIG. 65.—Actinomycotic abscess of human liver. Stained by Gram's method and safranin: ($\times 50$.)

- a.* Filamentous (streptothrical) form of the actinomyces embedded in a granular debris.
- b.* Portal space, with vein, bile ducts, etc.
- c.* Leucocytes and proliferating connective tissue cells around the fungus, these ultimately disintegrating and forming the pus of the abscess.
- d.* Unaltered liver tissue.

collections of cells many of them apparently polymorpho-nuclear leucocytes, others lymphocytes, both of which appear to be invading the tissues rapidly, and some large mononuclear cells. In the middle of most of these cellular masses a filamentous fungus may be seen, the filaments in the section under examination interlacing with one another and forming a more or less irregular network. In the immediate neighbourhood of the fungus the various cells appear to be disintegrated. Between the branching filaments is a clear homo-

geneous substance; this extends to the spaces between the cells of the tissue and the filaments, which therefore do not come into close contact. At the periphery of the mass are peculiar club-like bodies, the result apparently of the swelling of the outer sheath of the filaments, where they come into contact with the cells. This swelling is supposed to be protective (see § 502).

($\times 600$).—The branching filaments are readily distinguished, also the clear space around the organism, the numerous polymorphonuclear leucocytes and hyaline or mononuclear cells, some of which may contain fragments of the actinomyces. As the abscess formation proceeds, the proliferating connective tissue may be noted gradually invading and destroying the liver cells.

CYSTS OF THE LIVER

252. (1) Hydatid cyst usually occurs as a single cyst, though there may be several, in the right lobe of the liver. (See Hydatid Cysts under "Parasites" (§ 484).)

(2) Simple serous cysts are, as a rule, single; they are due, probably, to the distension of a bile duct, often brought about by obstruction from pressure of a cancer or some similar growth. As from all collections of bile in the liver, the bile salts, acids, and colouring matter are gradually absorbed, and a clear fluid is left.

(3) Similar cysts formed by the distension of bile ducts resulting from tubercular growths, softening and ulceration of their walls. These have a caseous and somewhat ragged lining, and contain a clear watery fluid.

(4) True cystic disease of the liver is often associated with a similar condition of the kidney. The cysts vary in size from microscopic spaces to cavities the size of a walnut. The walls are thin, smooth, and fibrous, and within the cavity a clear watery or serous fluid is collected. The mode of origin of these cysts is somewhat doubtful; some hold that they are formed by vacuolation of the liver cells, whilst others maintain that they are dilated bile ducts, the dilatation being caused by constriction of the ducts at certain points by a growth of fibrous and non-striped muscular tissues.

(5) A form of cyst said to be due to post-mortem decomposition, occurs, especially in hot weather (putrefactive emphysema). The liver tissue is converted into a kind of cavernous tissue by the rapid

formation, in its substance, of putrefactive gases. Nuttall and Welch ascribe this spongy condition of tissue to the action of the *Bacillus aerogenes capsulatus* which produces gas in large quantities in the dead or dying tissues. The organism appears to be distributed by the venous blood, and in the liver to give rise to large bubbles of gas which distend the venules and capillaries, ultimately causing them to rupture and forming regular cavities in the substance of the liver.

TUMOURS OF THE LIVER—HÆMANGIOMA

253. Hæmangioma is not very frequently met with in the human subject, but in the liver of the cat it is of common occurrence. When present it is usually found near the surface of the organ, and



FIG. 66.—Drawing from a section of a cavernous angioma of the liver. Stained with picro-carmin. ($\times 50$.)

- c.a.* Fibrous capsule marking off the angioma pretty sharply from the normal or fatty liver substance, *l.*
- f.t.* Fibrous trabeculae running from the capsule into the substance of the tumour, forming spaces (*c.s.*) lined with flattened nucleated cells (*e.*), and containing, apparently, nothing but blood—coloured (*r.b.c.*) and colourless (*l.*)—corpuscles.

may be seen shining through the capsule as a purple or dark claret coloured patch. The patch may be single, and about a third of an inch in diameter: or the growth may appear to be multiple. At the site of the tumour there is a slight depression, in which there is a

mass which has the appearance of an extravasation of blood sharply defined from the surrounding tissues, though it can be partially injected from any of the vessels of the liver. On making a section, after hardening a piece of the liver (§ 62 or 63) containing such an angioma, the tumour is seen to be rounded or wedge-shaped; it is sharply marked off from the liver tissue, at first sight appearing little more than a mass of coagulated blood. Stain (§ 102, 104, or 148) and mount (§ 195 or 199).

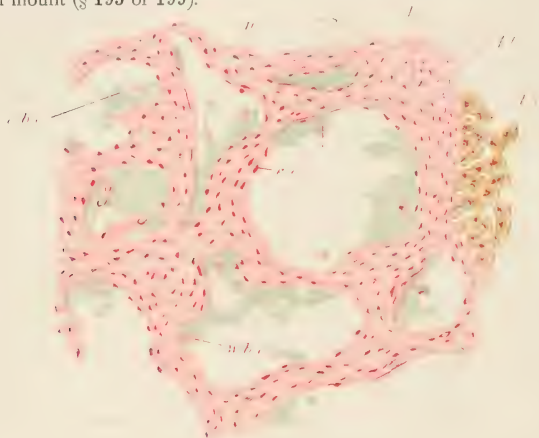


FIG. 67.—Drawing from a section of cavernous angioma of the liver.
Stained with picro-carmin. ($\times 300$.)

f.t. Fibrous trabeculae surrounding (*c.s.*) cavernous sinuses.

l.c. Nuclei of liver cells between sinuses, (*n.*) connective tissue nuclei.

e.c. Endothelial cells lining the sinuses, and in contact with

c.b.c. The coloured and (*w.b.c.*) the colourless blood corpuscles.

l.c. Liver cells at margin of the tumour.

($\times 50$).—Around the tumour, and circumscribing it sharply, as already seen, is a fibrous capsule, in which are numerous nuclei. Running in from this are bands or trabeculae of similar fibrous tissue stained pink, in which, again, the nuclei are deeply stained. The bands form a network, the spaces or meshes of which communicate with one another. In these spaces, under this power, a granular greenish mass (red blood corpuscles) is seen, with here and there a small pink dot (a leucocyte). This blood fills the cavernous spaces.

($\times 300$).—The delicate pink fibrous capsule and trabeculæ are seen; a large number of more deeply stained nuclei—of young fibroblasts—lie amongst, or on, the fibres. In some of the trabeculæ a few atrophied liver cells may be seen apparently enclosed and compressed between the bands of fibroid tissue; but in most of the bands there are no such cells. Lying on the bands of fibrous tissue, and evidently lining the cavernous spaces, are flattened endothelial cells, which, seen in section, are spindle-shaped; each cell contains one or more rounded nuclei. These cells have very much the appearance of the endothelial cells which form the smooth lining surface of blood vessels. Lying in the cavities are the coloured blood corpuscles stained yellowish-green, whilst here and there may be seen a hæmatein-stained cell, which will at once be recognised as a colourless blood corpuscle. These tumours appear to be formed by the dilatation of capillary vessels and atrophy of the intervening liver cells. The walls of the vessels become thickened, but in some places they give way, and additional intercommunications are formed. It appears, in fact, to be a condition similar to (but more advanced than) that described in “nutmeg liver” (§ 238).

OTHER TUMOURS OF THE LIVER

254. Tumours of the liver are similar in their structure to those found in other parts or organs of the body; here it will be necessary only to state what tumours may occur in this organ, and to give a few of their naked-eye characteristics.

Of the primary forms, malignant adenoma was first described by Greenfield, and it is probable that most of the primary cancers of the liver are of this form, which appears to be developed in connection with the bile ducts.

Malignant pigmented tumours of the liver are invariably sarcomatous.

Cancers, secondary to primary tumours of the breast, uterus, or alimentary canal, are of frequent occurrence; they may be either diffused or nodular. In the diffused form the liver is usually much enlarged, and markedly bile-stained. Throughout the organ there is a peculiar veining or mottling, caused by the presence of bands of glue-like material, very like the bands of young fibrous tissue seen in certain forms of cirrhosis, more especially to the naked eye, and in some cases even under the microscope. On more careful examina

tion, however, these bands are found to have a more or less characteristic carcinomatous structure. Of the nodular forms, the harder masses, sharply defined from the surrounding tissues, rounded but *umbilicated* in the centre, pink at the periphery, and yellower and fatty looking towards the centre, with, in some cases, fatty-looking patches, and but few hæmorrhagic points, are usually associated with scirrhus cancer of the pyloric end of the stomach. In some cases firm nodular sarcomatous masses are met with. These, however, are rare, and may usually be recognised by the presence of a larger number of minute hæmorrhages.

The softer nodules occurring in the liver may be either cancerous or sarcomatous, the latter comparatively rarely in adults. The liver is enlarged in both cases. They are both of rapid growth, and are sharply circumscribed; they project from the free or from a cut surface, are pink in colour, and, frequently, are somewhat translucent. The points of difference are, that in the sarcoma, (1) hæmorrhages into the tissues of the tumour occur more frequently—in consequence of this, red, brown, or yellow patches, according to the date of the hæmorrhage, are scattered throughout the substance of the tumour; and (2) there is no umbilication, while in the cancer this is almost invariably present.

Beyond the evidence to be derived from these general characters, it is, as a rule, impossible to collect, with the naked eye, any information which will enable one to state with certainty what is the nature of the tumour, and a careful histological examination (see Chapter XIV.) should always be made.

CHAPTER V

THE HEART

MICROSCOPIC STRUCTURE OF THE WALL OF THE NORMAL HEART

255. If a section be made through the wall of the left ventricle, and a thin layer of the tissue, embracing both the outer and inner surfaces, be prepared for microscopic examination (§§ 102, 103, 104, 195, and 199), the following appearances may be made out with the low power ($\times 50$). The epicardium, or visceral layer of the pericardium, is seen as a mass of pink tissue (with above stains), much more dense at its outer surface than near the muscular tissue, where we see an open connective tissue network, with distinct nuclei scattered throughout its substance. Bounding the muscular tissue is a layer of connective tissue, the cells of which are often infiltrated with fat. This layer of adipose tissue, almost invariably present, varies considerably in thickness, sometimes being exceedingly delicate. In the more open parts of the pericardium, sections of vessels are readily seen, and by special preparation, the presence of numerous nerves and lymphatics may be demonstrated. Beneath the pericardium are numerous bundles of yellowish-brown muscular tissue; in these bundles nuclei are seen lying between the muscle fibres. Bands of pink connective tissue run between the larger bundles of muscle fibre, and form a kind of supporting framework for the muscular tissue. The muscle bundles are seen in both longitudinal and transverse section. When the former, they appear as a reticulated mass of fibres, in some cases with meshes of considerable size.

On the endocardial surface are small elevations or irregularities—sections of the musculi papillares. The endocardium itself, under this power, appears to consist of a very thin layer of connective tissue, with here and there throughout its substance a few *small* bundles of

muscular tissue. Note also the somewhat pale bundles or fibres which underlie the endocardium proper.

($\times 400$).—The epicardium consists of ordinary connective tissue, with bands of yellow elastic tissue in the condensed part near the surface. Covering this is a single layer of flattened nucleated endothelial cells, which, seen in section, appear to be spindle-shaped; and beneath, as already seen under the low power, is a quantity of looser and more vascular connective tissue, beneath which again are the “signet-ring”-like fat cells, the nucleus in the angle of the cell being supposed to represent the seal.

The bulk of the muscle elements of the heart resemble those of ordinary striped or voluntary muscle, in that they are striated both longitudinally and transversely. Each fibre is composed of a series of muscle elements, each of which, in turn, is made up of the following:—(1) a nucleus containing an intranuclear plexus; (2) a thin film of what usually appears to be hyaline or more or less granular protoplasm, the two together forming the muscle corpuscle of Max Schultze, which is placed in the centre of (3) a series of striated, contractile fibrils, the functionally active part of the substance of the heart. This muscle (on treating as in § 44, 4 or 5) is broken up into a series of fragments or muscle elements, more or less cylindrical in form, each having for its central point a muscle corpuscle. The extremities of the muscle element are serrated, and in many cases at least one of its ends is bifurcated, each branch joining the serrated end of another, or part of another, element. When a number of these branching cylindrical muscle elements are examined *in situ*, it is seen that they make up the peculiar reticulated mass of fibres above referred to. On longitudinal section the cell is seen to consist of regular fibril bundles, “which take up stains deeply, and are separated from one another by clear undifferentiated protoplasm. This latter shows transverse lines at short intervals, which separate it into, compartments (sarcoplasmic discs), and these transverse lines correspond with definite transverse striæ on the fibril bundles (Krause’s membrane). The fibril bundles also show a broader transverse striation (Brücke’s membrane), which is not shared by the sarcoplasmic discs” (Cowan). On examining transverse sections the different fibres are seen to be of different diameters—in one case the section of a whole fibre is seen, in another the section of one of the branches only. Nuclei occupying the centres of the fibres are seen in transverse as well as in longitudinal sections, but only

when the plane of section happens to pass through the muscle corpuscle. If it passes through one of the branches only, or through the end of the muscle element, the nucleus cannot be seen through the mass of fibrils. At the poles of these nuclei (when the heart is from a subject over ten years of age, but especially if he be somewhat advanced in years), small accumulations of golden yellow or brown pigment may often be seen.

Around the muscle fibres of the heart there is no sarcolemma, and the highly vascular connective tissue which lies in the interstices of the muscular network is in direct contact with the muscle elements. In consequence of the peculiar spiral arrangement of the muscle fibres it is difficult to obtain any large series of fibre in longitudinal section. We have always sections through very various planes, except in the case of the papillary muscles, in which most of the muscle fibres run parallel to the long axis of the muscle.

The connective tissue has a rich blood vascular supply, entering from the pericardial surface and terminating at the endocardial surface and at the apices of the papillary muscles, and is completely honeycombed by lymph spaces and lymphatic vessels. The nuclei of these various tissues are readily seen in stained sections (§ 106 or 110 (*b*)).

On the inner surface of the endocardium is a single layer of flattened nucleated or endothelial cells. In the human heart this layer is seldom seen, as the organ is usually not removed within twenty-four hours after death, by which time the endothelial cells have disappeared. Beneath this layer is a network of small flattened, branched cells lying on a stratum of elastic tissue, and from it trabeculae run to join the connective tissue between the muscle fibres, whilst in its substance are to be found muscular bands some of which, though small, are in all other respects similar to those found in the myocardium, whilst others are thin non-striped muscle fibrils similar to those found in the uterus. These latter are very unequally distributed.

The network of irregular fibres, Purkinje fibres, found under the endocardium of the surface of the musculi papillares has assumed special importance as the fibres of which it is made up are supposed to be continuous with what is known as His's bundle or the auriculo-ventricular band, a bundle of paler muscular tissue which, arising in the right auricle from the so-called auriculo-ventricular node near the mouth of the coronary sinus, after passing into the interventricular septum divides into two branches, the right septal division of which,

in the sheep, is found running through the moderator band in the right ventricle and in the human heart in what Keith calls the great trabecula on the septal wall (part of which trabecula represents the moderator band of the typical mammalian heart) which runs between the attachment of the anterior group of the muscoli papillares and the pars membranacea septi below the right coronary aortic cusp. If a careful dissection be made along this line the bundle of pale fibres may be traced running in the line of the great trabecula up to the point mentioned below the right coronary aortic cusp. In the right ventricle, passing to the other extremity, it runs towards the apex, "where it divides into numerous fine threads terminating in the muscle fibres" (J. Mackenzie, who bases his account on Tawara's researches). A bundle of similar pale muscle fibres (the left division of the auriculo-ventricular bundle) passes over the muscular interventricular septum forming in section a kind of saddle-shaped bundle appearing in the left ventricle. In order to see these fibres in section it is necessary to cut out the portion of the base of the septum behind and passing through the base of the septal cusp of the tricuspid auriculo-ventricular valve along with the central fibrous "Knoten," as it is called by Tawara. It is, therefore, immediately under the right coronary aortic cusp and above the base of the septal cusp of the tricuspid valve. The cells which form these fibres are irregular in form, many of them being long and narrow (non-striped or involuntary muscle tissue), while others are more rounded and irregular. These latter may have one or more nuclei, and are striated at their edges or periphery; the interior of the cells consisting of undifferentiated protoplasm, although the surface seems to be slightly striated (G. G. Ellett). In the auricular fibres which pass from the bundle upwards in the intraseptal portions of the bundle the component fibres are thin and fusiform. In the ventricular part of the bundle, and as it is distributed over the surface, the cells are somewhat larger, are not so distinctly striated, especially in the centre, and usually contain several nuclei. This bundle in the left ventricle "rapidly widens out into a thin band which passes down to the apex, splitting into fine branches." The auriculo-ventricular bundle is distinctly separated from the ordinary heart-muscle tissue by a covering of connective tissue, which may be made out very clearly in sections stained by Mallory's or van Gieson's connective tissue stain (§ 168*a* or 103). This is seen, not only on the main bundle and in the bundle that runs along the septal wall in the

left ventricle, but also as it runs in the right ventricle. As soon as the bundles reach the network on the surface of the muscoli papillares this encircling connective tissue disappears so that around the superficial fibres of Purkinje there is no such sheath. It is important to make some little study of this auriculo-ventricular bundle and its relations as, under certain conditions, it appears to undergo fatty or fibroid degeneration, a condition associated with irregularity of the rhythm contraction of the auricles and ventricles of the heart.

CLOUDY SWELLING

256. Cloudy swelling of the muscle fibres of the heart appears to be the result of an inflamed condition of the myocardium maintained for a short time; in some cases, however, it may be looked upon as the precursor of fatty metamorphosis of the muscular tissue. It frequently occurs during the course of certain specific or organic fevers, where toxin is developed, as in typhoid fever, scarlatina, septicæmia, and similar conditions. In one case a severe burn, causing death in six hours, is recorded by Weber as having induced this condition in the muscle fibres of the heart and in the epithelium of the tubules of the kidney.

Naked-eye appearances.—The heart loses much of its firmness and toughness. Its muscular wall is softened, and in some cases even friable, and may be broken down fairly easily on squeezing it between the tips of the fingers and thumb. The tissue is of a dirty grey colour, in place of the usual purple red, and appears as though it had been slightly boiled (Perls). A fresh section of the muscle presents the same grey colour, and has a peculiar translucent appearance. Harden a piece of the muscular tissue, about three-quarters of an inch square, from the wall of the left ventricle (§ 62 or 63), examine one section unstained (§ 41), and stain others (§§ 102, 103, 104, or 109 *et seq.*, 132, and 135).

($\times 50$).—In longitudinal section the spaces between the individual fibres of the network are somewhat smaller than in the normal heart. This is especially the case near the endocardial surface. Even under this power the fibres look slightly opaque. Find a thin part of the section and centre it.

($\times 400$).—In the unstained specimen the fibres are somewhat opaque. The transverse striation, which in the normal fibre is so

distinctly marked, is lost, or obscured, and in place of it there is a granularity of the whole of the formed or striated material of the muscle element. The granules are exceedingly minute, and the appearance of the striated muscle is described as seen through a thin layer of dust or a sheet of ground glass. In such cases the nucleus is obscured and in certain cases it cannot be distinguished.

If instead of using a neutral solution in the examination of fresh tissue a drop of water be added to a few of the fibres spread out on a slide, the granules disappear, and the nucleus becomes distinctly visible. Again, if a drop of acetic acid is run under the cover-glass from the edge, the granular appearance fades away, and an almost normal-looking fibre remains.¹

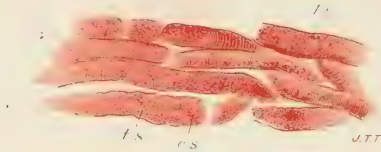


FIG. 68.—Muscle fibres of the heart in a state of cloudy swelling. Stained with picro-carmine, and mounted in Farrant's solution. ($\times 300$.)

- c.s.* Part of fibre in a condition of advanced cloudy swelling; transverse striation lost.
- t.s.* Indistinctly marked transverse striation.
- f.c.* Commencing formation of small fat globules.

Ether, chloroform, or strong alkalies run under the cover-glass in the same manner leave the cloudiness unaffected.

Examining the osmic acid stained specimen, nothing is found which cannot be observed by the above methods, as with this reagent there is no blackening of the fine granules; from this fact it is to be inferred that they are not yet of a fatty nature.

Picro-carmine, logwood, and van Gieson's stain do not stain the muscle elements deeply; but they are useful for bringing into prominence the nuclei of the interstitial tissue and of the muscle corpuscles.

¹ If a heart in which there is a cloudy swelling (especially in the early stages) be kept in alcohol for some time, the cloudiness may be diminished or may disappear. The alcohol appears to abstract water from the tissues, or otherwise so to change the protoplasm as to restore the refractive indices of the various elements to the normal.

The nuclei of the connective tissue are frequently more numerous and more deeply stained than are those in the normal heart, especially where the condition is examined at an early stage of the process of inflammation. These nuclei are then seen as deeply stained bodies lying between the bands of muscle fibres, arranged most frequently along each side of the small blood vessels.

This cloudiness of the fibre is not equally distributed throughout the wall of the heart, but is much more advanced in some places (usually near the endocardial surface) than in others. This is specially the case where the cloudy swelling is to be looked upon as the precursor of fatty degeneration.

FATTY INFILTRATION OF THE HEART

257. Fatty infiltration of the heart, or adipose heart, must be carefully distinguished from fatty degeneration of the muscular walls of the heart. In fatty infiltration there is at first simply an increase in the amount of the epicardial fat to which reference has already been made (§ 255). Subsequently, the fat extends from the epicardial surface into the muscular wall of the organ between the bands of fibres. Although the two processes of fatty infiltration and fatty degeneration are frequently associated (as in cases where the pressure of the invading adipose tissue on the muscle fibres appears to cause their degeneration), it will be well to describe the two conditions separately.

The adipose heart, as seen with the naked eye, appears to be larger than normal, the increase in size being due mainly to an increase in the amount of subpericardial fat: there is usually some flabbiness of the muscular tissue, more especially near the outer surface. Small yellow streaks run down in the somewhat pale muscular tissue, evidently merely continuations of the adipose tissue from the subpericardial layer. Unless there is also advanced fatty degeneration, the flabbiness does not extend beyond the gross lines of fatty tissue.

Harden (§ 63), cut (§ 82 *et seq.*), stain (§§ 102, 103, or 104, and 135), and mount (§§ 195 or 199).

($\times 50$).—The epicardial tissue is infiltrated throughout with fat, the connective tissue cells being distended with fat, and looking like the fat cells of ordinary adipose tissue; the highly refractile globules have a double outline, and are stained black with osmic acid or orange with Sudan III. The nucleus is situated at one angle of the cell, and

is stained blue, pink, or olive green, according to the stain used. These large cells extend in rows for some distance between the muscle fibres, but are entirely outside them; the condition is, in fact, one of

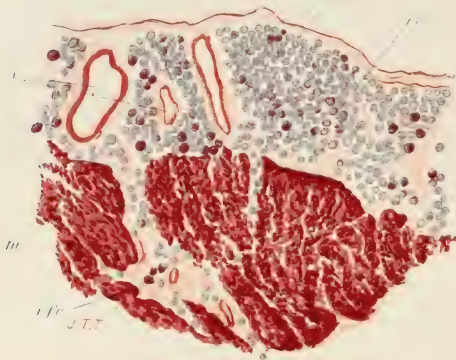


FIG. 69.—Section of adipose epicardium. Stained with osmic acid and carmine. ($\times 40$.)

e.c. Superficial epicardium. *f.c.* Deeper layer, enormously thickened, connective tissue cells distended with fat.

v. Vessels. *m.* Muscular tissue.

i.f.c. Fatty infiltration of connective tissue between the muscular tissue near the surface of the heart.

fatty infiltration of the connective tissue framework of the heart, and not of the muscle substance proper. In very marked cases this fatty infiltration of the connective tissue cells may extend as far as the endocardial surface, when, however, it is almost invariably associated with true fatty degeneration of the muscle fibres.

($\times 400$).—The cells of the adipose tissue are closely packed together, and the following parts may be observed in each. The protoplasm of the cell forms a mere film, except at one point or angle, where there is usually a triangular mass of protoplasm containing a nucleus, which, when stained, stands out very distinctly. Surrounded by the thin wall of protoplasm is a large, strongly refractile globule with a double outline, clear in the centre, but with a dark ring at the margin, or the reverse, according to the part that is focused. With picro-carminé the globule remains unstained, but with osmic acid it is stained black, or with Sudan III., orange. Between the muscle fibres

they have exactly the same appearance; in no way do they affect the fibre itself, except by actual mechanical pressure. As before stated,



FIG. 70.—Fatty infiltration of the connective tissue between the muscle fibres of the wall of the heart, stained with Sudan III. and hæmatein. ($\times 300$.)

f.c. Large fat cells between the muscle fibres.

m.f., m.f. Muscle fibres—slight fatty degeneration.

v. Small vessel filled with blood.

this condition must be carefully distinguished from fatty degeneration, which is an affection of the muscle substance proper.

FATTY DEGENERATION OF THE MUSCLE WALL OF THE HEART

258. Fatty degeneration occurs in patients who have succumbed to various exhausting diseases, such as phthisis, anaemia, leucocythæmia: to Addison's disease, or to certain diseases in which there is a deteriorated condition of the blood. It occurs also as a sequel to diseases of the scarlatina type, and to various septic conditions. Lastly, it is met with in patients who have died from phosphorus or arsenic poisoning, or in a minor degree, from alcohol, antimony, and sulphuric ether poisoning (§ 233). In some few cases, fatty degeneration appears to be due to the partial occlusion of the coronary arteries, affected with endarteritis deformans which has extended from the aorta, or to some other obstructive lesion. It also occurs as a sequel to endocarditis and pericarditis.

To the naked eye the heart has a characteristic appearance. It is somewhat dilated; on section it is pale and smooth, especially near the endocardial surface, which is considerably paler than normal. In the left auricle the endocardium is too thick to allow of the fatty patches being distinguished. As a rule, this pallor is not equally diffused over the whole surface, but appears in patches, especially in the musculi papillares and the columnæ carneæ. Unless the disease is advanced there may be little or no naked-eye evidence of its presence; it seldom extends to the pericardial surface.

On examining one of the musculi papillares, taking it as a typical specimen of an affected part, it is found that there are numerous small cream-coloured areas, or minute buff or yellow points, which stand out distinctly from the reddish-brown background. This has been very aptly compared to a "thrush's breast," and also to "faded leaves." These thrush's breast patches are usually transverse to the papilla and often run in zigzag lines or irregularly. In very advanced cases the cream-coloured patches have spread so far as to meet one another at many points, in which case the "thrush's breast" simile does not hold good. Where the degeneration is due to phosphorus or arsenical poisoning, or to scarlet fever, or leucocythæmia, small hæmorrhages are frequently seen immediately beneath the epicardium. The muscular tissue is flabby, and slightly, or in some cases very, friable, so much so that the thumb and fingers may be easily pushed through the muscular wall.

Harden (§ 62 or 63), stain, and mount (§§ 38, 103, 109, 132, and 135).

($\times 50$).—Very little is to be discerned beyond the fact that the muscle fibres appear in some cases to have become slightly enlarged. This is especially the case where the fatty degeneration follows upon an inflammatory condition: but in the pure degeneration, such as that brought about by metallic poisoning, the fibres are seldom increased in size. The enlargement of the fibres cannot be definitely determined, but it should be remembered that as the fibres increase in size the spaces between them become somewhat narrower, and the contained tissue elements more crowded together.

($\times 300$ or 400).—The nuclei between the muscle fibres are usually increased in number and distinctness. The transverse striation of the fibres has, to a great extent, become obscured; in some not a trace of it can be seen, whilst in those in which the change is not so far advanced the striation is seen only at the margins of the fibres. Ir

such cases where the centre of the muscle element of the fibre is most affected, the transverse striation is replaced by a number of small round granules or globules, which never, however, reach even a medium size. These granules and minute globules first make their appearance at the poles of the muscle corpuscles (the oval mass of protoplasm with its nucleus in the centre). From these points the process gradually extends through the length of the fibre, until, eventually, the whole of it is involved. The fibre then appears to consist of a series of rows of



FIG. 71.—Muscle fibres of the heart. Fatty degeneration. Section stained with osmic acid and mounted in Farrants's solution. ($\times 300$.)

- f.* Muscle fibre in which there is slight dimming of the transverse striation.
- f.c.* Small fatty granules and globules along the lines of longitudinal striation, especially around the nuclei and near the centres of the cells.
- a.* Blood vessel between muscle fibres. Note well-defined endothelial cells.

small round granules and globules, each row corresponding, more or less, to one of the fibrillæ of which the fibre is made up, so that at this stage the fibre, though perfectly well defined, has lost its transverse striation, and appears to be built up of rows of small, highly refractile bodies (like so many strings of beads). "Indeed, Brücke's lines are here and there replaced by minute black granules, each surrounded by a narrow line. In an early stage the granules are irregularly scattered throughout the cell, but in a more advanced condition several adjacent compartments

may be affected, but always those belonging to the same fibril bundle, and in the next stage the sarcoplasmic discs between the adjacent dots have disappeared, and two or more coalesce, forming an oblong" (Cowan). This condition resembles cloudy swelling in many respects, but may be distinguished from it by the following features: the granules and globules are larger, and, in the section stained with osmic acid, are black or brownish-black, or with Sudan III., orange, which is not the case with the granules in cloudy swelling. On the other hand, the fatty degenerated muscle is unaffected by a drop of acetic acid run under the cover-glass from its margin. Treated with chloroform, ether, etc., the fatty material is dissolved, whilst the granules of cloudy swelling

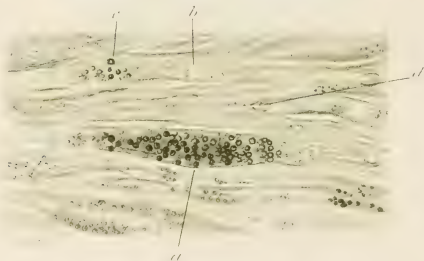


FIG. 72.—Muscle fibres of a heart taken from a case of advanced pernicious anæmia. Well-marked fatty degeneration. Section stained with osmic acid. Mounted in Farrant's solution. ($\times 300$.)

- a. Fibre in which there is advanced fatty degeneration. Oil globules much larger than usual.
- b. Healthy part (nucleus well seen).
- c. Fatty part of same fibre.
- d. Nucleus of muscle corpuscle in a comparatively healthy fibre.

remain unaffected. The transverse striation in this condition may be almost lost. As already noticed, the fatty degeneration occurs in localised patches, and as the section is examined under the high power, the same fibres may be fatty in parts, whilst in others they are to all intents and purposes healthy. With the microscope these areas can be localised much more accurately than with the naked eye. This degeneration usually occurs at the periphery of the circulation, *i.e.* at the distal area of the arterial supply. When we have to do with a simple case of malnutrition, the fatty degeneration may be distant from the vessels, but when we have a toxic agent at work, the degeneration is often seen in the immediate neighbourhood of the small blood vessels.

Fatty infiltration is frequently associated with fatty degeneration. In fact, as already pointed out, the infiltration when extensive may so compress the muscle fibres that their nutrition and function are very seriously interfered with, and a degenerative change in their substance is brought about.

PIGMENTARY DEGENERATION, OR BROWN ATROPHY OF THE HEART

259. This condition, again, is met with most frequently as the result of general wasting disease, where the process of exhaustion has been long continued. Consequently it is often found associated with fatty degeneration of the muscle in such conditions as phthisis, or more markedly still in Addison's disease. Uncomplicated brown atrophy is frequently met with in the hearts of old people; but marked pigmentation is often present in hypertrophied hearts.

The naked-eye appearances vary somewhat in different cases. When it is found in connection with atrophic conditions, the heart is dark brown in colour and smaller than normal, the walls are thinner, the cavities are contracted, the coronary arteries tortuous and more prominent than usual, and the epicardium is frequently thrown into folds. If the condition is unaccompanied by fatty degeneration, the muscle may be firm or even tough, or it may be "brittle"; but when associated with that condition, it is friable and soft, in which case, too, there are buff or yellowish patches scattered over the dark brown background. Where it occurs along with hypertrophy, the colour is not so dark, the tissue is firmer, and it may be that few of the characteristic features of the atrophic form are present.

Harden (§ 61, 62, or 63), mount a section unstained (§ 195), and another stained (§§ 103 or 109 and 199). A section taken from a heart removed from a patient affected with Addison's disease is described below.

($\times 50$).—The fibres are thinner than normal, and are not so closely packed as in the healthy heart. They are considerably broken up, the constituent muscle elements or muscle cells, with their serrated ends, being separated by intervals more or less marked in different places. Near the centre of each muscle element is a dark brown spot; if a bundle of fibres is examined in transverse section, a similar dark spot may be distinguished in most of the fibres, occupying the centre of the section of the fibre.

($\times 500$).—Where the pigmentary degeneration is unaccompanied by fatty degeneration, the transverse striation of the fibres is extremely well marked. The end of the segments, into which the fibres are divided, are distinctly serrated. In the centre of the segment the largest mass of pigment is observed occupying the position of the muscle corpuscle in and around which it is collected, especially towards the poles. In relation to this it will be remembered that even in the normal heart there is a small quantity of golden-brown pigment collected at each pole of the muscle corpuscle. So far, then, there is simply an



FIG. 73.—Brown atrophy of the heart. Muscle fibres broken up into short segments. Mounted, unstained, in Farrant's solution. ($\times 400$.)

- a.* Fibres splitting up into short detached fragments.
- b.* Pigment collected around the nucleus.
- c.c.* Pigment scattered along lines of longitudinal striation.

It will be noted that the transverse striation is very distinctly marked in this condition.

exaggeration of a normal process. Where the condition is advanced, as in the section now under observation, the pigment appears in elongated patches, following more or less regularly the lines of longitudinal striation. These patches are not confined to any part of the muscle element, but are more frequently seen at some distance from the periphery than near the margins. The granules of which the patches are composed vary, slightly, in size, but all alike are of a beautiful golden-yellow colour, when seen under a high power and by a strong light. In a transverse section of one of the muscle fibres the pigment is seen as a golden-yellow mass, occupying the centre of

the section of the fibre, whilst the smaller masses appear as minute points scattered throughout the substance of the fibre. In a stained specimen the nuclei may, in some few instances, be seen; but in most of the fibres the accumulation of pigment is so great that the nucleus is completely obscured.

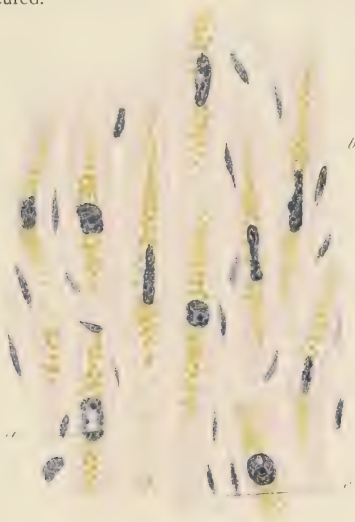


FIG. 74. —Brown atrophy of the heart. Stained with haematein.
($\times 500$.)

- a.* Nucleus of muscle corpuscle surrounded by
- b.* Non-striated muscle plasma in which granules of golden-brown pigment are collected.
- c.* Capillary blood vessels with well-marked endothelial lining and containing rows of red blood corpuscles.

The pigment is some altered form of hæmoglobin; but whether there is an accession from the blood, or whether there is simply a concentration of the pigment already in the muscle, is, as yet, merely a matter for conjecture.

ACUTE MYOCARDITIS

260. Acute myocarditis may occur either as a primary or a secondary condition, but it occurs much more frequently as the latter, extending

from the epicardial or endocardial surface into the substance of the muscle proper, or along the course of the connective tissue framework which supports the muscular structure. The presence of acute myocarditis is suggested by the symptoms during life, and after death by the

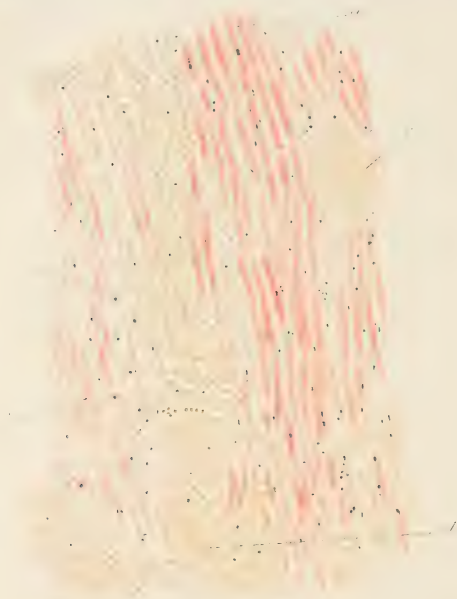


FIG. 75.—Acute hæmorrhagic myocarditis. Stained with alum hæmatein and picro-erythrosin. ($\times 60$.)

- a.* Swollen muscle fibres in a condition of cloudy swelling.
- b.* Isolated and atrophying muscle fibres.
- c.* Transverse section of blood vessel.
- d.* Blood extravasated into substance of heart wall separating fibre, etc.
- e.* Mononuclear cells. A few leucocytes may also be seen.

racemose reddening of the endocardium, the friability, the deepened colour, and the yellow patches on, or mottling of, the muscular wall. Harden (§ 62 or 63) and stain (§§ 103, 104, and 135). In very acute cases (septic) abscesses similar to those already described (§ 229) are found in the ventricular wall.

($\times 50$).—The fibres are swollen and packed closely. If the disease has been very acute, small areas of extremely opaque bluish-grey (or pink) material are scattered throughout the yellow muscular tissue; between the individual fibres, or around the smaller vessels, are numerous very small, deeply-stained points (nuclei). In some cases regular hæmorrhages may be seen between the muscle fibres, which are often widely separated from each other.

($\times 400$).—The bluish-grey areas are composed of swollen and bulging fibres which have lost all trace of striation; they present the appearance of broken-down, glassy-looking protoplasm (the result of the so-called vitreous degeneration), having in some parts almost angular depressions and bulgings; or the muscle fibres are now broken down, and there is simply a mass of more or less granular débris. These are the fibres in which the degenerative process is taking place most rapidly; some of the yellower-looking fibres appear to be quite normal, whilst others are in an advanced state of cloudy swelling (§ 256). The nuclei in the connective tissue spaces are considerably increased in number, most of them (leucocytes) lying around the vessels from which they appear to have emigrated. Some of the nuclei, however, are those of the connective tissue cells, which in this condition, being stimulated, are undergoing rapid proliferation. The vessels are usually somewhat dilated, and considerable collections of red blood corpuscles, the result of extravasation, are present in great numbers. In the section stained with osmic acid not a single black granule can be distinguished, showing that, as yet, fatty degeneration has not set in. If the condition is not so acute, and the patient has survived rather longer, the black reaction with the osmic acid may usually be observed at certain points in the mass of extremely granular débris.

CHRONIC INTERSTITIAL MYOCARDITIS—FIBROID DEGENERATION

261. The more chronic form of myocarditis, which is rather an interstitial inflammation than an inflammation of the muscle, like most of these diseases, is found usually on the left side of the heart, and especially in the wall of the left ventricle. The muscular wall is firm and hard, and cannot be broken down with the fingers as can the muscle of a normal heart. Distributed through, or sometimes almost replacing the muscle fibre, especially near the apex, are grey, semitranslucent or yellowish-opaque fibrous bands or patches to which the tissue owes its

firmness. These are especially numerous at the apices of the musculi papillares, which are there often shrunk and deformed. The septum may be similarly affected, as also "the posterior wall of the left ventricle about the junction of the upper and middle thirds." These patches, as a rule, are most marked in the body of the muscle, and usually do not extend to the epi- or endocardium.

There appear to be at least two distinct forms of this interstitial myocarditis—one (*a*) in which the primary change is an increase in the delicate connective tissue that surrounds the muscle fibres and supports



FIG. 76.—Muscle fibres from a heart in which there was acute myocarditis. Stained with picro-carmin, and mounted in Farrant's solution. ($\times 300$.)

- a.* Fibres, comparatively healthy, in a condition of cloudy swelling.
- b.* Fibres broken down into an almost granular mass. These fibres are slightly but irregularly swollen.
- c.* Parts of the fibres as yet only in the condition of cloudy swelling. These are placed between parts which are in the more advanced stage of disintegration.

the blood vessels. This appears to be followed by a gradual wasting and supersession of the muscle fibre, and occurs as the result of the action of poisons met with in the course of certain diseases, *e.g.* syphilis. (*b*) A form in which, in consequence of the cutting off of the blood supply, there is more or less rapid atrophy and degeneration of the muscular tissue; as this degenerated muscle is absorbed it is gradually "replaced" by new fibro-cellular connective tissue. Harden (§ 61, 62, or 63), cut (§ 94), stain (§§ 103 or 110(*b*) and 132), and mount (§ 199).

Under the microscope the principal change observed in the first instance is probably a more acute process, in which there is prolifera-

tion of the intermuscular connective tissue cells, this being followed by



FIG. 77.—Fibroid degeneration of heart. Stained with alum hæmatein and van Gieson's stain. ($\times 30$.)

P.C. Pericardial surface. Fatty or adipose tissue containing numerous blood vessels.

m.f. Bundles of muscle fibres, with new fibro-cellular tissue (*f.c.*) running in between them, especially where the muscle fibres are wasted. New tissue may be thickened perimysium.

e.ob. Transverse section of artery in an advanced stage of endarteritis obliterans.

e.c. Endocardial surface, beneath which are bundles of very small muscle fibres.

Note the cellular infiltration around the small blood vessels, giving rise to thickening of the adventitia.

the development from the new tissue of fibrous bands, often of consider-

able thickness, which intersect and compress the muscle tissue proper, in which case we have what is known as fibroid degeneration of the heart. The connection between the acute and chronic forms is very similar to that described as existing between acute interstitial hepatitis and common chronic cirrhosis.

($\times 50$).—In the early stages, lines or accumulations of cells with deeply stained nuclei, following pretty closely the lines of the perivascular lymphatics, are seen. In some cases these nuclei form bands almost as broad as the bands of muscular tissue. The smaller vessels are often increased in size, and their walls, especially the adventitia, undergo considerable thickening. In the later stages this cellular tissue has, except immediately around the blood vessels, given place to well-developed dense fibrous tissue, with a few scattered, deeply stained nuclei. These fibrous masses are often of considerable size, and in them atrophied patches of muscular tissue, sometimes fatty, but more frequently pigmented, may be seen. Usually, the fibrous tissue has running through it a few small blood vessels, the walls of which are somewhat imperfectly developed.

($\times 400$).—The muscle fibres may be perfectly normal in appearance, but between them the deeply stained nuclei are very numerous, and the dilated blood vessels, with their thickened walls, are also well seen, the thickening being due, chiefly, to an increase in the number of cells in the adventitia. Where the condition is more chronic, or where the patient (say in acute rheumatism) pulls through the first stages of the disease, the young cells become organised into fibrous tissue, which stains pink with picro-carmin, or with the van Gieson stain, and in which are seen a number of spindle-shaped fibroblasts. Where this stage is reached, the muscle fibres are usually undergoing atrophy and sometimes fatty degeneration, though neither of them is by any means invariably met with. These conditions appear to be due to malnutrition of the fibres, brought about, first, by the altered condition of the blood which has induced the cell proliferation, and, second, by the mechanical pressure of the newly formed fibrous tissue on the muscle fibres. The fatty fibres are similar in appearance to those previously described (§ 258). A condition spoken of as cardiac sclerosis is described by Cornil and Ranvier, in which the essential details are similar to those above described. It occurs very frequently during the course of interstitial nephritis, more especially in patients who are at the same time suffering from maniacal symptoms.

In a heart in which there is aneurism at the apex of the left ventricle (by far the commonest position), the muscle fibre usually undergoes extensive local softening, such as fatty degeneration, myocarditis or endocarditis; it may be the result of acute (rarely of chronic)



FIG. 78.—Syphilitic interstitial myocarditis. Stained with alum hæmatein and alcohol eosin. ($\times 200$.)

- a.* Transverse section of muscle fibres.
- b.* Longitudinal ditto.
- c.* Wasting muscle fibres.
- d.* Small blood vessel surrounded by small mononuclear cells.
- e.* Fibroblast in new connective tissue between wasted muscle fibres.
- f.* Endothelial cells.
- g.* Plasma cell.
- h.* Mononuclear cell.
- i.* Granules of pigment (*i*) in atrophied muscle fibres.

myocarditis, or of stoppage or obstruction of the blood supply through emboli (infarction) or diseased coronary arteries. Even in the aneurisms near the base of the heart, in the interventricular septum, the muscle fibres in the immediate neighbourhood usually undergo fatty degeneration.

($\times 30$).—A section made completely through the heart wall in a case in which this second form of fibroid degeneration is well marked is of great interest, in so far that in it may be seen a considerable number of small arterioles in which there is well-marked endarteritis obliterans, the lumina being almost closed. As a result of the interference with the supply of nutrient blood to the muscle, there is evident wasting of the muscles, and a corresponding development of new fibro-cellular connective tissue. Around the minute vessels a number of nuclei are seen, some of them belonging to new connective tissue cells, a few to polymorpho-nuclear leucocytes and lymphocytes. Near the epi- and endo-cardia the muscle tissue is not so much wasted, the nutrition being maintained on the one hand by the anastomosing vessels in the epicardium, and on the other by the blood derived directly from the heart cavity. Hyaline, fatty and pigmented, atrophied muscle fibres may be seen surrounded by the new, and “replacing” connective tissue in which yellow elastic fibres are numerous.

($\times 150$).—In a section from the muscle of the wall of the left ventricle in a case of “fibroid degeneration” resulting from embolus or thrombosis of a branch or branches of the coronary artery, the wasting and degeneration of a patch of muscle fibre is seen. Around the blood vessels and between the wasting fibres the nuclei of the new “replacing” connective tissue can easily be made out. The muscle fibres, highly dependent upon a full blood supply, waste and degenerate, whilst the connective tissue, stimulated by the dying tissue which in this respect acts almost like a foreign body, and still receiving sufficient blood to supply its less exacting requirements, grows vigorously, and as elsewhere fills up the gap that is left when the muscle is absorbed.

ENDOCARDITIS

262. The structure of the endocardium has already been briefly described (§ 255). The results of endocarditis are most evident in connection with the valves of the various orifices, and it will be well to see what parts of (and in what proportions) the endocardium enter into the structure of the valves. The layer of flattened connective tissue cells, with the fibrillated tissue and yellow elastic fibres, which has already been described as lying immediately under the layer of endothelium, is continuous from both the auricles and the ventricles on to their respective valves. The endothelial covering is also con-

tinuous, and is further prolonged over the chordæ tendineæ, which are composed of yellow elastic and white fibrous tissues, and any process affecting the surfaces of the valves is most frequently continued along the chordæ tendineæ. The aortic and pulmonary valves are, in the same manner, covered with a layer of endothelium, that of the heart becoming continuous with that of the vessel, and the subjacent condensed layer of fibro-elastic tissue of the one becoming continuous at the margin of the valve with that of the other. Modified and non-striped muscle fibre is sometimes met with in these positions.

ACUTE ENDOCARDITIS

263. Acute endocarditis is seen in patients who have succumbed during the early stages of an attack of acute rheumatism, scarlet fever, or pneumonia; more rarely, it may be associated with phthisis, cancer, gout, or Bright's disease. The most marked evidences of the disease take the form of small verrucous or warty growths, which are found along the lines of contact of the valves, chiefly in the left heart, on the mitral and aortic valves—the former on the auricular aspect near the margins, the latter on the ventricular aspect, and at some little distance from the margins of the cusps. These warty growths are much more rarely met with on the tricuspid and pulmonary valves, but when they do occur the same rules as regards their position hold good. The growth or vegetation is “soft, friable, and semi-transparent.” In the more acute form it never reaches any very great size, but smaller growths occur all along the points of contact of the valves. If separated from the valve, a small portion of the subjacent tissue is brought away, leaving an ulcer the size of the base of the vegetation. If the patient has survived the early stages of the disease, the growths may increase considerably in size, but they have much the same structure as the smaller forms. Along with these vegetations, at the points of contact of the valves, others may occur on the whole of the auricular surfaces of the valves, the process radiating from the primary focus. The chordæ tendineæ, which, as already observed, are simply continuations of the endocardial covering of the valves, are very much swollen, and extremely brittle.

Harden a piece of a valve, on which is a typical vegetation (§§ 58 and 62 or 63). Cut sections (§ 94) through the vegetation and the valve at right angles to the plane of the valve. Stain (§§ 103, 110(*b*), 132, and 117.)

For full description of these vegetations, see § 226, but here note that ($\times 300$) the cells of the endocardial tissue appear to have undergone proliferative changes, and that from them most of the tissue composing the base or pedicle of the growth arises; the proliferation is so rapid and so great that, just as in the case of a granulating wound, the mass of cells passes beyond the level of the endocardium, and a small projection is the result. The yellowish mass on the surface is made up of two elements, degenerating cells and coagulated fibrin, both of which may be readily distinguished with the aid of picro-carmin (§ 102) and other stains.

In the section stained with methylanilin-violet, a number of micrococci may sometimes be seen, forming a deeply stained granular layer on the surface of the disintegrating cells and fibrin. In ordinary acute endocarditis these micrococci do not appear to give rise to any serious changes, even when they are carried off, along with parts of the disintegrating mass near the surface, to give rise to minute embolic infarcts in other organs.

CHRONIC ENDOCARDITIS

264. As in the case of all other inflammatory processes, acute endocarditis tends to become chronic—especially if not extremely acute at the commencement. The vegetations occurring in the positions already mentioned then become firm, hard, fibroid masses, having a broad base; they are not so prominent as in the acute form. The edges of the valve are thickened, especially along the lines of contact. At certain points the thickened valves have become adherent at their extremities by the organisation of the inflammatory products, and are usually puckered and retracted. As in the case of acute endocarditis, the valves of the left side of the heart—the auricular surface of the mitral valve, and the ventricular surface of the aortic valve—are the parts specially affected. The right side is only affected where the disease commences whilst the child is still *in utero*. In some few cases the thickening extends from the valves to the walls of the cavities. The chordæ tendineæ are shortened, thickened, and opaque, and look almost like pieces of firm cartilage. In place of being brittle, as in the acute form, they are extremely tough. In the mass of thickened fibroid tissue, calcareous plates may frequently be observed immediately under the endothelial cover-

ing, or pultaceous or fatty granular material may occupy the same position.

Harden (*a*) one of the valves, on which is one of the flattened vegetations, and (*b*) one in which are fatty and calcareous patches (§ 62 or 63), and stain (§§ 103 or 104 and 110 (*b*)).

($\times 50$).—In place of the round cells which, in the acute form, were observed in the vegetation, and in the endocardium beneath it, there are now a number of spindle-shaped or flattened cells, fibroblasts, the nuclei of which take on nuclear stains. Between these fibroblasts are layers of fibrillar substance arranged in regular lamellæ, giving rise to the appearance of a very much thickened endocardium. This lamellated tissue is stained pink with picro-carminé or fuchsin, and has all the characters of fibrous tissue. On the surface of the vegetation there is frequently a deposit of fibrin, but it is usually freshly deposited, and does not stain, although the few cells entangled in the fibrinous meshes are deeply stained. This fibrin has therefore been deposited whilst the blood current was slowing, and as the patient was dying. In fact, in almost all sections of vegetations examined, any deposit of fibrin on the surface appears to have been deposited, in great part, during the last few days of the patient's life.

Examine the section in which are the fatty and calcareous plates ($\times 300$). In the spaces originally occupied by the flattened cells, there is now more frequently a mass of yellow granular material. In the deeper endocardial layer this granular material is replaced by a number of highly refractile granules, which, on the addition of a drop of hydrochloric acid, evolve bubbles of gas (carbon dioxide) and then disappear. These highly refractile granules, then, are small calcareous particles deposited in the fatty material. In some few places the fibrous tissue is also undergoing fatty degeneration and calcareous infiltration, as a result of which large calcareous patches have been formed. In the very early stages, however, the change is confined to the spaces in which the flattened cells lie, the intercellular fibrous tissue being stained a beautiful pink. This condition should be studied along with endarteritis deformans, to which it bears a very close resemblance (§§ 271 and 272) especially in the more chronic forms in old people, when it occurs on the aortic surface of the semilunar valve. The vegetation in the early stages might be compared to a mass of granulation tissue growing on a free surface, that of an ulcer, for example. In the later stages the vegetation may be likened to the fibrous cicatrix which is left

when the ulcer has healed. If such tissues are examined together, it will be seen at once how closely the two stages of the one correspond to the two stages of the other.

ACUTE ULCERATIVE ENDOCARDITIS

265. This condition, which in many respects resembles the acute form of endocarditis already examined, and is by many writers considered to be the same disease, differs from it, apparently, in the two following points:—1st, that it is more destructive in its local action, especially where there is strain or friction; and 2nd, that the fragments detached and carried into the circulation give rise to a much more rapid and widespread mischief than do emboli from the simple acute form. To the naked eye the vegetations appear to be very similar to those described in the simple form, but they tend to occur more indiscriminately over the endocardial surface of the valves or of the heart wall and in the lower reaches of the aorta. They also appear to be much more liable to break down and to leave ulcerated patches. The vegetation itself, taken, for example, from a case of ulcerative endocarditis occurring during the course of a case of pyæmia, if stained and examined as described for the acute form, will be found to present exactly the same character under both low and high powers, as already described (§§ 226 and 264), the micrococci in the superficial layer being especially well seen. Harden (§ 58), stain (§§ 103, 110 (*b*), 132, 117, and 135).

($\times 50$).—The floor and margins of the ulcer are infiltrated with a great number of small round cells, which take on the nuclear stain, except at the surface, where there is a distinct yellowish tinge, which points to the fact that the tissues are here undergoing degenerative changes. In the section stained with osmic acid this same area appears to be much darker than the deeper tissue.

($\times 300$).—The stained cells are closely packed together, forming the floor and margins of the slight depressions or roughened elevations. Directly in contact with the blood is a layer of extremely granular cells, the granules in some cases appearing almost like small globules. This layer is stained more or less yellow with the picro-carmin or van Gieson stain, and the small globules (which are often free) and granules are stained black with osmic acid. Here, too, small quantities of free blood pigment may be seen. Mixed with this layer of degenerated tissue is a quantity of granular-looking fibrin, in which, in a section

stained with methylanilin-violet (§ 117), may be seen colonies of micrococci, some of these colonies being of considerable size. It is



FIG. 79.—Section of endocardium, etc., from a case of ulcerative endocarditis—*Staphylococcus aureus* infection. Stained by Gram's method with Bismarck brown contrast stain. ($\times 40$.)

e.c. Endocardial surface. Here is a mass of fibrin with a number of leucocytes, and, covering the whole, a layer of staphylococci stained with gentian-violet. Near the endocardial surface the muscle fibres are separated by new or proliferating connective tissue.

m.f. The deeper muscle fibres with very little interstitial infiltration,

probable that most of these forms of endocarditis are the result of the action of micro-organisms.

SIMPLE PERICARDITIS (see § 222)

PURULENT AND TUBERCULAR PERICARDITIS

are also sometimes met with. In the latter form, the covering of lymph is usually of great thickness, is yellow, and has pus on the surface. On microscopic examination tubercle follicles with large well marked giant cells are seen throughout the new fibrinous layer, but they are specially numerous near the surface of this layer.

NEW GROWTHS MET WITH IN THE HEART

Tubercle in the pericardium (rarely in other tissues), syphilitic gummata, secondary cancers and sarcomas (rarely primary), fibroma, myoma (congenital), and lipoma. (See Chapter XIV.).

CYSTIC PARASITES

Hydatids of *Tænia echinococcus* (§ 484), and *Cysticercus cellulosæ* of *Tænia solium* (see § 481).

CHAPTER VI

BLOOD VESSELS

NORMAL HISTOLOGY

266. Capillary vessels consist simply of a single layer of more or less flattened endothelial cells. Each cell contains a nucleus, by the double rows of which, in section, the capillary vessel is most easily recognised. Between the cells is a cement substance, which is stained brown with nitrate of silver. The cement substance is supposed to have considerable pathological importance, for, as we have already seen, in the process of inflammation where the vessels are distended, the cement substance may give way, and openings or stomata, through which the coloured and colourless blood corpuscles escape from the vessel, are said to occur in it.

Around some of the capillaries there is a second sheath, sometimes spoken of as the perithelium, which is composed of "a network of branched connective tissue cells" (Klein). Between these two layers is a reticular or fibrillated layer, which is of great pathological importance, as it is in the fibrils (forming a kind of basement membrane) on which the epithelial and perithelial cells rest that the process of waxy degeneration occurs.

267. A medium-sized artery is made up of three layers or coats—the "tunica intima," the "tunica media," and the "tunica adventitia."

The tunica intima is composed (1) of a layer of endothelial cells, very similar in appearance to those already described in the capillaries; (2) subendothelial connective tissue or intima proper, which consists of longitudinal and transverse laminated tissue with branching connective tissue cells lying between its layers; (3) the so-called internal elastic lamina, an elastic homogeneous layer, which is usually wavy owing to the contraction of the muscular tunica media of the wall,

this contraction taking place during the hardening of the vessel. It is composed of interlacing bands of elastic tissue, between which are openings or fenestræ; through these the vessels of the media may make their way into the lumen of the vessel during the process of organisation in a thrombus.

The tunica media, the middle or muscular coat, is composed of non-

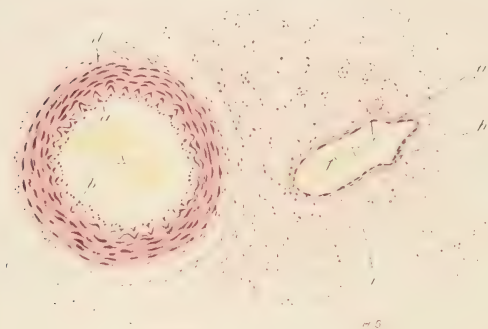


FIG. 80.—Transverse section of normal artery and vein. Stained with alum carmine. ($\times 50$.)

- A.* Artery, with (*a.*) lining nucleated endothelium resting on a delicate laminated connective tissue.
- b.* Internal elastic lamina thrown into folds by the contraction of
- c.* The thick muscular coat, composed of non-striped muscle fibres, the nuclei of which are seen as deeply stained rod-shaped nuclei.
- d.* Fibro-cellular adventitia.
- V.* Vein, with (*e.*) flattened endothelial cells.
- f.* Thin intima.
- g.* Thin muscular coat.
- h.* Fibro-cellular adventitia.
- i.* Fatty tissue.

striped muscle fibres, arranged, principally, transversely to the axis of the vessels. Where more than one layer is present, they are arranged regularly, rod-shaped nuclei being seen in the fibres. Between the individual layers of non-striped muscular tissue are laminæ and networks of elastic tissue; in the larger vessels these elastic laminæ are especially prominent. Vasa vasorum are found passing from the

connective tissue of the outer coat, the tunica adventitia, for some distance into the substance of the media, the capillaries of these vessels stopping short at the part of the coat next the endothelial lining of the intima, which rarely receives capillaries from this source. In the smaller vessels the adventitia is in direct contact with the media, but in the larger arteries there is an elastic network similar to that already described but not so thick, and spoken of as the external elastic lamina, separating the two coats.

The tunica adventitia or outer coat is composed of connective tissue, with numerous cells, between which are bundles of pink-stained (with picro-carmin or the van Gieson stain) fibrous tissue, with, here and there, especially near the media, longitudinal bundles of yellow elastic fibres; the elastic laminae are stained yellow. Small vessels invariably run and ramify in the adventitia of the larger vessels to supply the walls with nutriment.

268. The structure of the aorta differs somewhat from that above described. The adventitia is comparatively thin; the media contains relatively little muscular tissue; the internal elastic lamina of the smaller vessels is here represented by a number of thin layers of elastic tissue intersecting the muscular tissue, networks of elastic and connective tissue running along with the vasa vasorum between thin layers of muscular tissue. Here, too, the intima is thicker than in any other vessel; it is composed of an endothelial layer and a thickened sub-endothelial layer, in which are numerous flattened nucleated connective tissue cells, resting on a layer of reticulated elastic tissue.

The coats of the veins correspond to those of the arteries, but here the adventitia is the most prominent of the three; the tunica media is composed of irregular bundles of non-striped muscular fibre, with little or no elastic tissue, simply a basis of connective tissue; the various parts of the intima are very delicate. The valves of the veins appear to be merely folds of the intima, in which a portion of the muscular coat is invaginated.

In all vessels numerous lymph spaces lined with endothelium are found in the adventitia, and, in the larger vessels, tubular lymphatics in the same position. Lymph spaces between the bundles of muscular tissue are also met with, probably associated with the vasa vasorum; these communicate with the lymph spaces of the adventitia.

HYALINE DEGENERATION

269. During the course of certain specific infective fevers, typhoid fever, scarlatina, and septicæmia a peculiar hyaline degeneration of the "corneal" coat lying between the endothelial lining of the artery and the internal elastic lamina is met with. This condition has been carefully described by both Klein and Greenfield as occurring in the arterioles of the kidney during the course of acute inflammations of that organ, and by others in the arterioles of the spleen during the

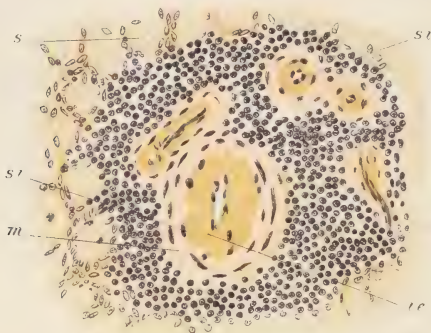


FIG. 81.—Section of small branch of splenic artery undergoing hyaline degeneration. Stained with hæmatoxylin, rubin, and orange. ($\times 300$.)

- a.* Adenoid tissue of Malpighian body.
- i.e.* Endothelial lining of vessel.
- s.i.* Swollen and hyaline tunica intima.
- m.* Tunica media or muscular coat of vessel.
- s.* Splenic sinuses—arterial.

course of the above diseases. To the naked eye there is little to call special attention to this condition except that in both kidney and spleen there is evidence of acute inflammation which in the spleen takes the form of acute congestion of the pulp tissue and an abnormal prominence of the greyish Malpighian bodies. Harden (§ 56, 58, or 63), cut (§ 82 or 94 *et seq.*), and stain (§ 147 or 148).

($\times 50$).—The pulp sinuses are larger than normal, and are distended with blood. The sections of the nodes of perivascular adenoid tissue known as Malpighian corpuscles stand out very distinctly from the

congested pulp tissue, the lymphocytes are numerous and closely packed together, whilst in each "corpuscle," sometimes in the centre of the mass of lymphoid tissue, sometimes placed eccentrically, is a vessel in which there is distinct swelling of the laminated connective tissue; this forms the greater part of the intima of the vessel. The endothelial cells may also be swollen, but their nuclei are usually deeply stained. The fibrous trabeculae in the spleen are also somewhat swollen, and may have a hyaline or glassy appearance.

($\times 300$).—The exact localisation of the hyaline swelling can now be made out. The nuclei of the endothelial cells stand out prominently; the sharp line of demarcation between the swollen laminated intima and the muscle fibre of the vessel is also well seen. In smaller vascular branches the hyaline swelling is readily traced; the pulp sinuses are fully distended with blood corpuscles. In the kidney the process is seen best in the afferent arterioles of the glomeruli, especially at the point where the vessel enters Bowman's capsule. The swollen and hyaline tissue takes on the stain of degeneration. This condition should be studied alongside vessels in which waxy or amyloid degeneration is taking place (§§ 274, 288, and 289).

ACUTE ARTERITIS

270. This form of inflammation is met with principally in the aorta, but it may also occur in the smaller vessels, especially in those near wounds. In the aorta *the naked-eye appearances* are very characteristic. On the inner surface of the first part of the aorta, especially near the coronary arteries, are one or more patches of soft elastic or gelatinous-looking material of a yellowish colour, or, it may be, of a pearly pink appearance. The patches vary in size, but are usually from a quarter of an inch to half an inch in diameter, and are sharply defined from the surrounding intima, which is almost normal, or only slightly swollen and thrown into small folds in the immediate neighbourhood of the swelling. The outer surface of the vessel is usually inflamed at this point; a mass of semi-gelatinous or oedematous-looking tissue, having a pink tinge, is seen, from all of which it is evident that the acute endarteritis is accompanied by periarteritis. In some cases the tunica media is also swollen and infiltrated.

Harden (§ 62 or 63), cut sections transversely to the long axis of the aorta (§ 82 or 94 *et seq.*), and stain (§§ 103 or 110 (*b*) and 132).

($\times 50$).—Where the thickening is marked, the cells of the deep layer of the intima, undergoing rapid proliferation, are extremely numerous, and are separated only by thin layers of the laminated tissue. Even where the thickening is as yet not well marked, flattened cells, with somewhat elongated nuclei, may be seen in the deeper layers. All these cells take on nuclear stains readily.

Where the condition is advanced, there is also an increase in the number of cells in the adventitia; the increase in some cases becomes so marked that the adventitia looks almost like a mass of granulation tissue. In some few cases small, round, deeply stained cells are scattered through the muscular tissue, but usually the middle coat is little affected.

($\times 300$).—The cells in the intima, immediately under the endothelial lining, composed of nuclei, surrounded by thin films of protoplasm, all give evidence of great vegetative activity. Their growth is maintained at the expense of the fibrous laminae. In the deeper layers, or where the process is not so far advanced, the flattened nucleated cells may still be seen, but they are cloudy and granular. In the adventitia the capillary vessels are more prominent and are distended, and new loops may frequently be seen shooting through the media into the thickened intima. Along the course of these vessels, which may be seen as double rows of flattened cells, are numerous small round cells, some composed of little but a nucleus, others having around the nucleus a quantity of protoplasm. As these cells are developed, and the connective tissue fibrils and yellow elastic fibres are swollen, softened, and absorbed, the wall of the vessel may become considerably weakened.

Where these patches occur in minute vessels, aneurisms may result from the wall of the vessel giving way at the weakened point. (Acute Multiple Aneurisms, §§ 275 and 276.)

As in all cases where there is a formation of granulation tissue, as the process becomes more chronic, there is almost invariably a formation of fibrous tissue. This occurs especially around the mouths of the branches of the aorta,—*e.g.*, in the coronary arteries, which are frequently surrounded by constricting bands of fibrous tissue formed by the organisation of the round-celled tissue; all this leading to obstruction of the blood vessel, interference with the flow of blood, degeneration of the muscle of the heart wall, and the formation of new interstitial fibrous tissue. (Fibroid Degeneration, § 261.)

CHRONIC ENDARTERITIS—"ENDARTERITIS DEFORMANS"—
"ATHEROMA"

271. This may be described first as it occurs in one of the smaller vessels, and then as it occurs in the aorta. It is found especially in the vessels of aged people, and is to be looked upon as a degenerative process, following a low form of inflammation. In the vessel (one of the larger vessels at the base of the brain) from which the section described is taken, are patches of opaque, pale, firm tissue, in some cases quite hard and gritty when cut, scattered at irregular intervals along the course of the vessels.

These patches vary from one-sixth to one-third of an inch in length, and are usually confined to one side of the vessel, so that on section one side of the vessel wall is seen to be much thicker than the other, the lumen being eccentric. On cutting into these masses, they are firm, hard, and in many cases calcareous and gritty feeling, but some of them "cut" almost like cartilage or fibrous tissue; frequently they are softened and yellow in the centre. The lumen is very much narrowed in places, whilst at one part the vessel is completely blocked by a clot of blood which has become adherent to the thickened and roughened wall.

Harden (§ 60, 62, or 63) and stain (§§ 103, 110 (*b*), and 132).

($\times 40$).—The wall of the vessel is unequally affected. The change takes place almost entirely within the internal elastic lamina which may be recognised as a wavy yellow line (with picro-carminic or van Gieson's stain) situated immediately within the muscular layer, this latter being known by its regular lamination and the rod-shaped nuclei. The patches are very unequally distributed on the wall of the vessel, so that in transverse section the vessel has somewhat the appearance of a signet-ring.

At the point where there is least change we have simply a thickening of the laminated part of the intima, in which there is proliferation of the flattened cells which lie between the fibrous laminae. There appears to have been no proliferation of the endothelium. From this point the thickening gradually increases until it is very marked, involving about half the circumference of the vessel. Where it is most marked, the intima may split into two layers, each of which is composed of laminated, fibrous-looking tissue; between the two laminae is an open space. It will perhaps be advisable to examine the different layers, from the lumen to the intima, in order.

Near the lumen the fibrous tissue, as in the thinner part, is well stained, showing, occasionally, the nucleus of a flattened cell. The cells in this position are increased in size and take on stains very readily.

Beneath this layer comes a mass of similar flattened laminated tissue, but the spaces in which the cells lie are much larger; the cells



FIG. 82.—Section of one of the medium-sized cerebral vessels affected with chronic endarteritis deformans (atheroma). Stained with logwood and eosin. ($\times 40$.)

- a.* Thickened tunica intima.
- b.* Internal elastic lamina.
- c.* Muscular tunica media.
- d.* Tunica adventitia.
- e.* Endothelial lining covering
- f.* Localised thickening of the tunica intima.
- g.* Two small points at which calcification has occurred. Immediately around the calcareous patches the nuclei are present in considerable numbers.

are very granular, and do not quite fill the spaces. In the deeper part of this layer, these spaces usually run into one another, and are filled with a bluish-grey, highly refractile material, which disappears on the addition of hydrochloric acid, with the evolution of bubbles of carbon dioxide. Then comes a mass of homogeneous-looking material, stained—but very unequally—in which are numerous irregular slits or openings running in all directions, which contain granular or semi-

crystalline bodies identical in appearance with those in the more regular spaces. Some of the irregular openings are of considerable size, and contain granular debris in addition to the bluish-grey material. In most cases the line of demarcation, formed by the internal elastic lamina (between the diseased and the healthy tissues) is very distinct; but in the more advanced condition this bounding lamina has given

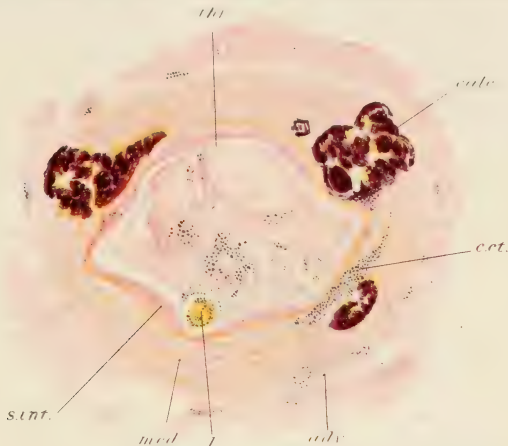


FIG. 83.—Extreme atheroma of pudic artery, calcareous degeneration of muscular coat. Stained with alum hæmatein and picro-erythrosin. ($\times 35$.)

- l.* Channel along which blood could pass.
- thr.* Thrombus.
- s.int.* Irregularly thickened tunica intima.
- med.* Normal muscular tissue of tunica media.
- adv.* Tunica adventitia with some cellular infiltration.
- c.ct.* Small nutrient artery surrounded by inflammatory cellular infiltration.
- calc.* Calcified mass in muscular coat.

way, and a process similar to that described in the deeper layers may be observed in the tunica media, the muscular layer becoming broken down and atrophied.

In a logwood-stained specimen very similar details come out, but the nuclei near the lumen are much more prominent than are those in the deeper layers.

In certain cases the muscular coat appears to be affected much



FIG. 84.—Section of a medium-sized vessel (cerebral artery), endarteritis deformans. Stained with picro-carmine. ($\times 250$.)

- a.* Placed in the lumen of the vessel.
- b.* Small round cells immediately under the lining endothelium.
- c.* Thickened intima, with flattened laminae, and flat cells (corneal structure), cells and laminae both swollen.
- d.* Region in which cells and inter-cellular laminae are both becoming granular and swollen (fatty and calcareous deposit).
- e.* Broken down tissue, in which are large cracks and fissures, calcareous salts, crystals, etc.
- f.* Layer next to internal elastic lamina, similar in appearance and structure to *d*.
- g.* Yellow internal elastic lamina.
- h.* Muscular tunica media, perfectly healthy.

more than the intima (see section of pudic artery). Here there is comparatively slight but irregular thickening of the intima, so that the changes internal to the internal elastic lamina are not at all marked, with the exception of thrombus formation by which the lumen of the vessel is almost occluded. In the media, however, we have patches of inflammatory cells, and evidence of fatty degeneration and calcification. Here also there is some evidence of periarteritis in the increased number of cells in the large perivascular lymph spaces. This impaired nutrition of the media must be associated with the perivascular changes on the one hand and the blocking of the vessel on the other. There can be little doubt that under these conditions the circulation through the vasa vasorum must have been considerably obstructed.

($\times 300$).—The earliest indications of the advancing changes can be best made out immediately under the endothelium. The laminae, seen so distinctly under the low power, are separated from one another, the intervals being occupied by cells, which, near the surface, are numerous, rounded, and deeply stained, lying in rows between the separated laminae. Some of these are merely resting nuclei, others are undergoing swelling and proliferation, whilst others again are surrounded by a thin film of protoplasm. The laminae in this position are swollen. As the distance from the surface increases, the proportion of cells to fibres diminishes, the cells become flattened, they are not so deeply stained, and in many cases they are granu-

lar, the granular material becoming more abundant as the surface is left. These granules in the deeper parts are stained black by osmic acid. Later, a number of similar granules make their appearance in the swollen fibrous tissue. The spaces around the granular areas are much enlarged, as though they had at some time been distended; but now they contain only the débris of such tissue as originally caused the distension. When cells and matrix have both become granular, the whole mass may break down, and large spaces containing the calcareous-looking material (some parts of it granular, others crystalline) are seen. In some of the spaces or cavities a few crystals of cholesterin may be found; these are recognised by their shape and by the fact that



FIG. 85.—Cholesterin crystals. ($\times 200$.)

when a section is stained with iodine and then transferred to a weak solution of sulphuric acid (§ 134), they are stained blue, especially at their edges.

Where the calcification has passed into the middle coat, the appearance presented is exactly that seen in the deeper layer of the tunica intima—a homogeneous or granular matrix, in which are numerous large spaces containing granular débris and highly refractile crystals. This is usually accompanied by an increase in the number of cells in the adventitia, an indication that there is an accompanying condition of periarteritis.

In a section stained to bring out the elastic tissues (§ 167). ($\times 50$),

note, passing from the normal to the swollen intima. that in addition to the internal elastic lamina we have in the intima a series of wavy bundles of fibres which take on the blue stain. As the thickening becomes marked it will be seen that one bundle keeps near the lumen, a few fibrils only passing into the new tissue. Then comes a second bundle

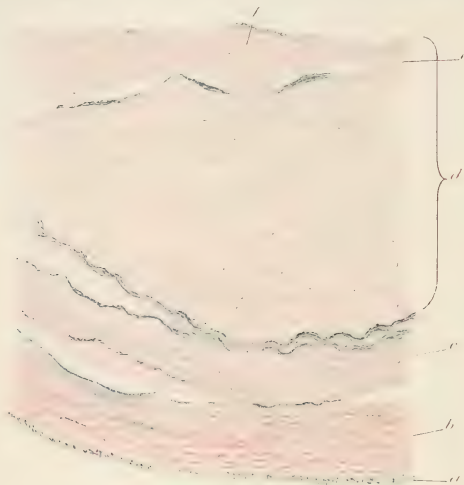


FIG. 86.—Section of atheromatous artery. Stained by Weigert's method and with alum carmine. ($\times 50$)

- a.* Fragments of the tunica adventitia and external elastic lamina.
- b.* Middle or muscular coat.
- c.* Internal elastic lamina split into layers by new connective tissue growth.
- d.* Enormously thickened tunica intima, laminated connective tissue, more cellular than normal, with a few delicate elastic fibrils.
- e.* Denser bands of yellow elastic fibrils.
- f.* Inner portion of proliferating tunica intima. Modified endothelial layer and proliferated laminated connective tissue cells. Note layer of elastic tissue on the surface.

beneath which, again, are a few fibrils. Just within the internal elastic lamina are a series of wavy bundles, sometimes of considerable thickness, at others much thinner and more delicate looking, the internal elastic lamina thus becoming broken up by a kind of process of infiltration into a series of widely separated laminae, in place of a series of laminae

between which are simply a few connective tissue cells. Where the separation of the laminae is most marked the muscular tissue outside this layer appears to be elongated, the fibrils become thinned, the number of connective tissue cells becomes greatly increased, regular lines of such cells lying between the muscle fibres.

($\times 200$).—Confirm the above. There has been a remarkable, but slow and regular, proliferation of the cells between the elastic fibres, as the result of which there is a great increase in the amount of white fibrous tissue formed, apparently, by fibroblasts. As they grow and separate the elastic laminae, the elastic tissue becomes gradually broken up into short lengths, the loss of continuity of the bundles being a very marked feature. The changes in the adventitia are comparatively slight. The muscular tissue is, however, distinctly thinned not only as regards its whole mass, but as regards the fibrils of which it is constituted. The elastic fibrils between the bundles of muscular tissue sometimes become more prominent as the muscular tissue undergoes atrophic change. In the muscular coat much of the elastic tissue appears to be accumulated in the walls of the vasa vasorum, many of which may be seen running at right angles to the axis of the vessel, others parallel to it.

The principal points to be noticed are, that part only of the circumference of the wall of the vessel is affected, and that the change takes place in the subendothelial tissue, commencing as a swelling and proliferation of the cells, followed immediately by a swelling of the fibrous matrix. These in turn, and in the same order, undergo fatty degeneration and calcareous infiltration, the most marked changes taking place in the deepest layers of the swollen and proliferating tissue, and the most recent changes near the lumen of the vessel. The process commences near the internal elastic lamina, and extends through the intima towards the lumen of the vessel. Usually the internal elastic lamina defines, sharply, the diseased area, but this is not always the case; when the media is invaded, the adventitia may be affected, not only secondarily, but in some cases primarily.

ATHEROMA OF THE AORTA (ENDARTERITIS DEFORMANS)

272. *Naked-eye appearances*.—Endarteritis deformans is most frequently met with in the first part of the aorta, where, also, it is seen in the most advanced stage, but it may occur in any part of the vessel, often around the openings of its branches, especially about the orifices of

the branches springing from the arch, and then around the other vessels, in pretty regular order from above downwards. It appears to affect those parts of the aorta at which the strain is greatest, and the movement most continuous. For the sake of convenience it may be divided into four stages, but all the four stages may be observed in the same vessel. In the earliest stage the affected area is the site of a pale



FIG. 87.—Atheroma of the aorta. Stained with picro-carmine.
($\times 50$.)

- a.* Position of lumen of vessel.
- b.* Layer in which there is proliferation of cells and swelling of fibres.
- c.* Commencement of fatty degeneration.
- d.* Fatty degeneration and calcification in both cells and fibres.
- e.* Muscular and elastic coat.
- f.* Muscular and elastic coat teased out a little, to demonstrate the muscular and elastic layers.

(Note that here there is no internal elastic lamina.)

pinkish-opaque, translucent or opalescent, somewhat gelatinous-looking, swelling of the intima. Though these swellings vary considerably in size, they seldom exceed half an inch in diameter: they are rounded or oval, and have a perfectly smooth surface, so that they evidently lie beneath the endothelium which lines the vessel. In some cases these rounded patches lie so close together, that as they spread they meet

one another, and form irregularly shaped pearly masses, each of which very early acquires a yellow centre. On cutting into one of the swollen patches, at this stage, the pearly tissue is found to be firm and fibrous, whilst the yellow centre is softer and more readily broken down. The mass may remain firm and tough, but, as a rule, the softened yellow patch becomes larger until it comes almost to the surface; in this softened area calcareous salts are deposited, and eventually a calcareous patch is formed which is covered by a single layer of endothelial cells resting on a thin membrane of laminated tissue, these two together separating the calcareous patch from the blood stream. The swollen or calcareous patches may be separated from the tunica media with the finger-nail at almost any stage, leaving the media intact.

($\times 300$).—Examine the contents of one of these small softened centres. Spread out the fatty or cheesy-looking material on a slide in a drop of Farrant's solution (§ 195), and press a cover slip firmly down on it, with the handle of a needle. Note (1) fatty granules and shrivelled fatty-looking and granular cells and fibres; (2) highly refractile granules, which disappear on the addition of hydrochloric acid (calcareous granules) and reappear in the form of crystals when sulphuric acid is added; (3) fatty acid crystals; and (4) crystals of cholesterin, which may be recognised as rhomboidal plates, from one corner of which a small rhomboidal chip is wanting.

In more advanced cases the middle coat may be invaded, just as in the case of the pudic and cerebral arteries already described. Where this occurs aneurism very frequently results, owing to the weakening of the vessel, the media being the true resistant coat.

Harden (§ 60, 62, or 63), cut (§ 82 *et seq.*), stain (§§ 102 and 195, or 103, 104, and 167), clear (§ 193), and mount (§ 199).

($\times 50$).—The intima is now on the convex surface of the wall of the vessel; the elastic tissue in the media and adventitia causes these two coats to contract, and the outer surface of the vessel becomes the concave surface. The next point to be noted is that there is no distinct internal elastic lamina, and consequently no distinct line of demarcation between the intima and the media. In the media, as already stated, series of fenestrated elastic membranes separate the bundles of muscular fibre one from another.

Immediately under the endothelium, the appearances are very similar to those described in the smaller vessels, except that the cell proliferation is not nearly so well marked. Some of the spaces are

undoubtedly enlarged, and the once flattened cells have now become swollen and are proliferating. The fibres are also swollen. Passing down farther, the changes are still very similar, except that the granular and shrivelled-looking cells are arranged in more regular layers with the pink fibrous laminae between,—first a layer of cells, then a layer of fibres, and so on. Deeper still, the fibrous tissue also becomes granular looking; and lastly, just before the muscular tissue is reached, is seen a homogeneous yellow-stained layer, with calcareous material (black or bluish-grey) deposited in the cracks and spaces. These spaces vary very much in size; some are about two or three times the size of an ordinary cell space only, whilst others are so large that they occupy a considerable part of the thickened intima.

($\times 300$).—The flattened cells close to the surface are so granular that they appear to form long, flattened, regular rows of granules. Between these the fibrous tissue is swollen, but it is not markedly granular until the surface has been left for some little distance. After this the changes are almost identical with those noted in the smaller vessel, and the interpretation of the appearances is much the same. It will be noticed that in the earlier stages of the disease there is a layer of homogeneous delicately stained tissue intervening between the media and the lower and more advanced portions of disintegrating tissue. The changes take place in the following order, the most recent again being near the lumen, the more advanced nearer the internal elastic lamina. Near the endothelial layer we see swelling and proliferation of the deeply stained cells; then come swelling of the fibrous laminae, fatty degeneration of the swollen cells, and similar changes in the fibres. This tissue either breaks down at this stage, or there is a deposit of calcareous material, first in the cells, and then in the fibrous tissue. As these parts become fatty, they no longer take on the nuclear or fibrillar stain of picro-carmin or van Gieson's stain, but are stained yellow by picric acid. The calcareous particles are more highly refractive, and have a bluish-grey colour when examined under the high power. The fibrillar tissue intervening between the broken-down calcareous material and the intima is very frequently found to be undergoing fatty degeneration, and small oil droplets are seen throughout its substance, which, although not sufficiently numerous to affect the staining reactions, may be very readily seen scattered at intervals, either in or between the bundles of fibrous tissue. Further evidence of slight fatty degeneration may be seen in the interstitial tissue of the

media, in some few cases affecting the internal muscular fibres of that coat.

Stain a section to bring out the elastic tissue (§ 167), clear (§ 193), mount (§ 199), and examine.

($\times 50$)—It is seen that wherever the atheroma is well developed the intimal layer in which we have proliferation of the connective tissue

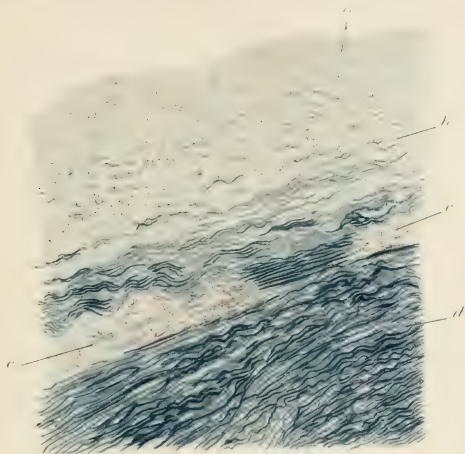


FIG. 88.—Section of atheromatous aorta. Stained by Weigert's method and with alum carmine. ($\times 60$.)

- a. Tunica intima, thickened superficial layer.
- b. Deeper layer of the tunica intima or superficial tunica media in which the elastic laminæ are separated by a new growth of cellular connective tissue, which soon becomes fibrillated.
- c. Irregular fibro-cellular patches "replacing" considerable areas of the yellow elastic tissue.
- d. Laminated yellow elastic tissue of the tunica media, between the strands of which nuclei of connective tissue cells may be seen.

cells and swelling of the fibres is almost entirely devoid of elastic fibrils. As we pass from the surface, in place of having the well-defined laminated bundles so characteristic of the deeper layers of the intima, there appears to be a marked separation of these bundles, which are broken up into short corrugated lengths with swollen white fibrils and a few cells lying between. Beneath this layer, again, are similar irregular

patches in which the elastic tissue has almost disappeared. These irregular patches vary in size, but always contain remains of the elastic fibrils, some of which may be seen to have been continuous (although the continuity is now broken) with the regular bundles in the immediate neighbourhood. In these paler areas little streaks of altered or granular blood pigment stand out considerably more prominently than do any in the areas in which the elastic fibrils are well developed and unaltered.

($\times 300$).—The proliferating cells and swollen white fibrils of the intima are now well seen, these being continued in between the bundles of elastic tissue as noted above. The extremely cellular nature of the deeper pale patches also comes out well under this power, the cells gradually apparently removing the elastic bundles, only small fibres of which can now be seen. The arrangement of the lines of pigment suggest, strongly, that these are merely the remains of altered blood lying in the obstructed vessels—the vasa vasorum.

ENDARTERITIS OBLITERANS

273. There is a more or less acute inflammatory process, which not only affects the laminated intima, but also involves the endothelial lining of the arteries. This condition occurs most frequently as (1) a syphilitic endarteritis; (2) the form which is found in healing wounds, in thrombosed vessels, and in interstitial inflammations, *e.g.* stone-mason's phthisis; and (3) a similar form, which is found in the vessels of the kidney during the course of Bright's disease (really a form of No. 2).

In syphilitic disease this endarteritis is of extremely common occurrence, and is, according to several authors—Heubner, Friedländer, Greenfield, and others—an important factor in determining the caseation of gummata in syphilitic interstitial growths. It occurs especially in the cerebral arteries—medium-sized vessels—but it may occur in smaller vessels in almost any organ of the body. In the basilar artery, for instance, so affected, small nodular thickenings are seen, the lumen of the tube affected becoming very irregular in shape and very much contracted. In some cases clots are found in the lumen, but these are frequently of post-mortem formation. Harden (§§ 60, 63), cut (§ 84 *et seq.*), stain and mount (§§ 102 and 195, or 103, 104, and 199).

($\times 50$).—The thickening is mostly in the intima, internal to the internal elastic lamina. At the same time there appears to be some

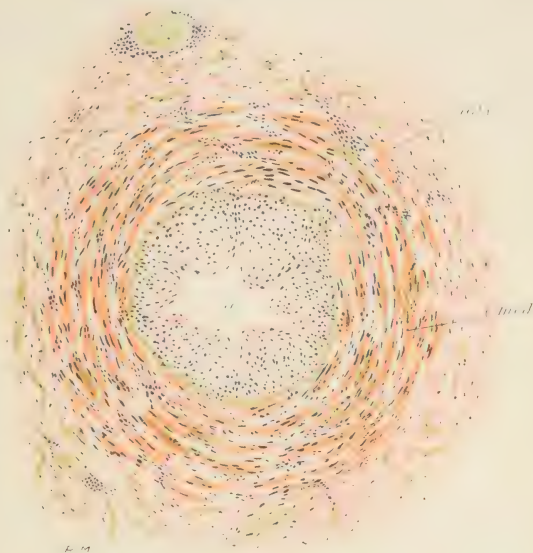


FIG. 89.—Arteritis—artery with thickened walls from a wound.
Stained with alum hæmatein and picro-erythrosin. ($\times 80$.)

- a.* Greatly and irregularly thickened tunica intima, due in part to proliferation of the lining endothelial cells.
- med.* Tunica media with marked cellular infiltration, following the lines of the small nutrient vasa vasorum.
- adv.* Thickened tunica adventitia in which similar cellular infiltration is seen.
- v.* A larger vessel (vein) with well-marked cellular infiltration.

slight infiltration of the adventitia with cellular elements, especially around the vasa vasorum. The middle coat is usually irregularly thinned.

The thickened intima is made up of numerous cells, which appear to be formed by proliferation of the endothelial cells, and of the flattened cells of the intima. As already stated, this proliferation may become so great that the lumen of the vessel may be almost obliterated.

($\times 300$).—Lining the vessel is a layer of more or less flattened cells,

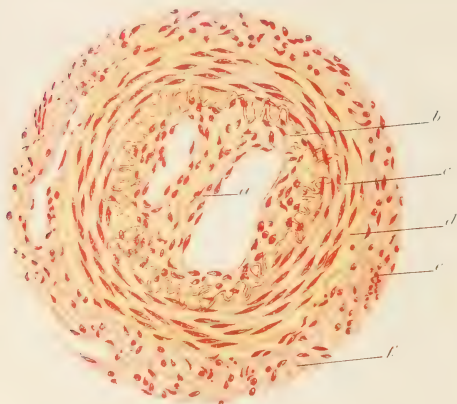


FIG. 90.—Section of small artery from the boundary area of the kidney from a case of subacute interstitial nephritis. Well-marked endarteritis obliterans. Stained with picro-carmin. ($\times 200$.)

- a.* Enormous thickening of subendothelial and endothelial tissues, the letter pointing to a process passing from wall to wall, and dividing the lumen into two channels.
- b.* Yellow internal elastic lamina.
- c.* Well-marked muscular coat.
- d.* Delicate external elastic lamina.
- e.* Fibro-cellular adventitia increased in thickness.
- f.* Epithelium of one of the straight tubules.

which are spindle-shaped or rounded when seen in section. Beneath this is a layer of irregular cells, some with rounded, others with elongated nuclei, whilst deeper still, and next to the internal elastic lamina, is a layer of flattened cells, with here and there a group of rounded cells. Pushing their way into this mass of cells are numerous capillary blood vessels, which pass through the internal elastic lamina,

from the capillaries of the inner layers of the media. It will be noticed at once that this is a process of organisation of a granulation tissue; and, as a matter of fact, we find that where the process has lasted for any considerable length of time, imperfectly developed fibrous tissue is formed. There is no fatty degeneration. Organisation in a clot in a

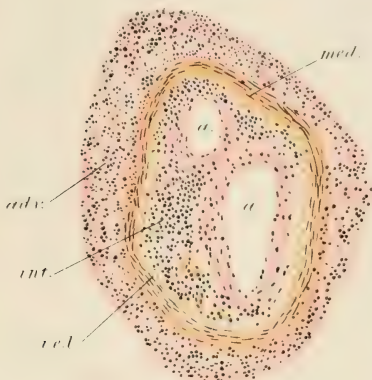


FIG. 91.—Section of cerebral artery showing syphilitic endarteritis obliterans. Stained with alum hæmatein and van Gieson's stain. ($\times 100$.)

- a.a.* Channels left representing the lumen of the vessel, near which are flattened cells representing the endothelial layer.
- i.e.l.* Internal elastic lamina.
- int.* Thickened and cellular inner coat in which small blood channels may be seen. Cells derived from internal cells by a process of proliferation.
- med.* Muscular coat *relatively* thin.
- adv.* Greatly thickened and very cellular tunica adventitia.

vessel differs in no essential detail from that described in the chapter on Inflammation, Organisation, and Repair (Chapter III.).

In almost all cases of *endarteritis obliterans syphilitica*, as in the similar condition in interstitial nephritis in stone-mason's phthisis, and in the endarteritis met with connected with the organisation of a thrombus and in a healing wound, there is marked thickening of the adventitia and even of the surrounding connective tissue. This

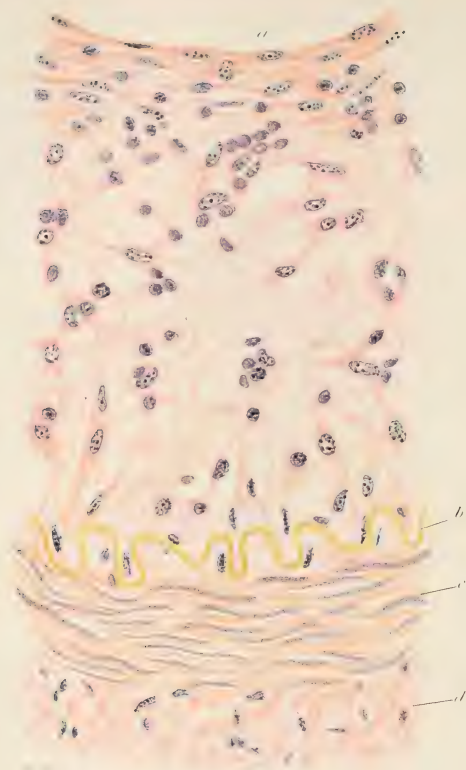


FIG. 92.—Drawing of small segment of section of a cerebral artery, syphilitic endarteritis obliterans. Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

a. Lumen of the vessel bounded by layers of proliferating endothelial cells.

b. Internal elastic lamina. Note the great similarity of the cells on each side of this membrane. These are probably endothelial cells lining small nutrient blood vessels (*vasa vasorum*).

Between *a.* and *b.* the intima is enormously thickened. In this thickened intima fibroblasts and mast cells may be seen in considerable numbers. Sections of small blood vessels (not usually present in the tunica intima) are well seen. These are lined with well-defined endothelial cells.

c. Muscular coat.

d. Adventitia; cellular and thickened blood vessels, *h.*, prolonged through the media, and into the deeper layer of the intima, *i.*

thickening consists either of a mass of small round cells, or of such a mass that has become organised into fibro-connective tissue, more or

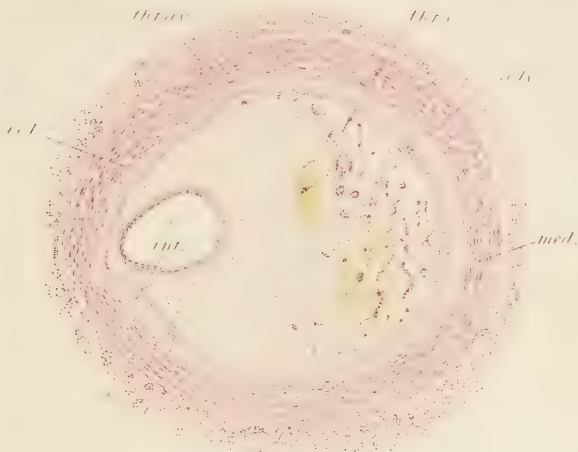


FIG. 93.—Organising thrombus in an artery. Stained with alum carmine. ($\times 20$.)

- adv.* Tunica adventitia with increase of cells around the vasa vasorum.
- med.* Tunica media—muscular coat.
- i.e.l.* Internal elastic lamina.
- int.* Tunica intima somewhat thickened, especially where the clot is being vascularised.
- c.* Channel in the thrombus.
- thr.av.* Portion of thrombus in which vascularisation is not going on.
- thr.v.* Thrombus in which lines of endothelial cells, young blood vessels, can be seen in longitudinal and transverse section. Remains of blood pigment are seen in this part of the clot.

less fully developed, which may be readily recognised under the microscope.

CHANGES WHICH TAKE PLACE IN THE MIDDLE COAT OF ARTERIES

274. Of these several have been already mentioned as occurring in connection with disease of the intima; an important one to be mentioned

here is calcification of the middle coat, which occurs especially in the medium-sized vessels of elderly people suffering from endarteritis deformans in the aorta. First there is fatty degeneration of the muscular wall of the artery; this makes its appearance in yellow patches or circles in the deeper part of the wall, and gradually spreads, but before the patches run together a deposit of calcareous material usually takes place in the yellow fatty rings. Later, the whole muscular



FIG. 94.—Drawing of a vessel (mesenteric) in which the middle coat is slightly affected by waxy or amyloid disease. Stained with methylanilin-violet. ($\times 600$.)

m.f. Circular muscle fibres of the middle coat, cut transversely.

w.c.f. Between the muscle fibres the connective tissue fibrils are swollen and waxy; stained red violet. Within the vessel the nuclei of the endothelial cells are readily recognised.

f.c. Fat cells.

wall becomes first fatty and then calcareous, when it is represented by nothing but a brittle tube. If this be macerated in dilute hydrochloric acid, a perfect cast of the muscular coat remains.

Harden (§ 62 or 63), cut (§ 82 *et seq.*), stain (§§ 103 and 135), clear (§ 193), and mount (§ 199).

($\times 50$).—The muscular coat is seen to be undergoing fatty degeneration, the tissue appearing yellow (with picro-carmin and van Gieson's

stain instead of brownish-yellow) or blackened (with osmic acid). The intima and adventitia are almost normal in appearance.

($\times 300$).—The tunica media is undergoing fatty degeneration at certain points, the muscle fibres and connective tissue are granular and much yellower than normal, whilst with osmic acid a number of the granules are stained black.

At other parts highly refractile calcareous granules are seen. These, when treated with hydrochloric acid, disappear, and carbon dioxide bubbles are evolved. The intima and adventitia are comparatively healthy, though the adventitia in some cases appears to become infiltrated with cells and to be considerably weakened; this latter condition usually follows rupture of the brittle tube.

A similar calcification often occurs in the smaller arteries, such as those at the base of the brain, where, however, the patches have a peculiar annular arrangement. The microscopic appearances of a transverse section are exactly the same as above.

Fatty degeneration of the vessels is met with in phosphorus poisoning (§ 233). It occurs especially in the capillary vessels, where the protoplasm around the nucleus first becomes granular; then droplets of fat are formed in the cells of which the wall of the vessel is built up. These droplets are stained black with osmic acid, and may come to occupy the whole of the cell. Punctiform hæmorrhages are found where the vessels have given way under increased pressure. The fatty degeneration may extend to the smaller arterioles, and, like the condition described in the next section, greatly predispose to the formation of aneurisms or even ruptures of vessels.

Waxy degeneration in the middle coat, the parts specially affected being the delicate connective tissue fibrils between the muscle tissue proper, which remains unaffected or undergoes merely atrophic and fatty changes, the result of malnutrition, is met with, especially in the small arterioles. (See descriptions of the waxy organs, §§ 237, 288, etc.)

CHRONIC PERIARTERITIS, OR INFLAMMATION OF THE TUNICA ADVENTITIA

275. Chronic periarteritis is usually associated with endarteritis, especially in interstitial inflammations of the kidney, lung, etc., in the accounts of which conditions it has already been described more or less fully. It is met with in syphilitic interstitial inflammations,

forming a marked feature in such cases ; but the most important form of the disease is that which occurs in the small arteries of the brain, where we have a chronic inflammation of the adventitia, usually associated with endarteritis, and a gradual atrophy and degeneration of the middle coat, evidences of which may be readily seen under the microscope. The outer coat is formed of laminae of fibrous tissue, between which the connective tissue cells may be seen as flattened corpuscles ; the middle coat becomes granular, and very much compressed and condensed. With this condition multiple aneurisms and hæmorrhages are frequently associated.



FIG. 95.—Cerebral arterioles on which are numerous miliary aneurisms the result of chronic arteritis. Stained with picro-carminé. ($\times 50$.)

To demonstrate these aneurisms, take a piece of the brain near which the hæmorrhage has occurred. Leave one of the large vessels attached, and holding this vessel with forceps allow a jet of water from a fine nozzle to play forcibly upon the broken-down tissue, until all the cerebral substance and blood are washed away and only a group of thread-like structures with small granules on them is left. These thread-like structures are the blood vessels of the brain, the granules the miliary aneurisms. The accompanying drawing gives a very good idea of the appearance of these aneurisms when stained (§ 102) and mounted (§ 195).

Whilst the blood vessels are under consideration, it may be well

to give, very briefly, the various forms of aneurisms which are met with as a result of injury to, or disease of, the walls of the vessels.

TRUE ANEURISMS

276. A true aneurism is a dilatation of a vessel as a result of which a kind of sac is formed; the walls of this sac consist of some or all of the coats of the vessel, but usually of parts of the intima and the adventitia only. The blood is thus kept within its proper walls, but not within its proper bounds. Anything which weakens the wall of the vessel, such as endarteritis, slight injury, overstrain, etc., predisposes to this condition.

The wall of an aneurism is composed almost entirely of laminated fibrous tissue. Between the laminae are flattened cells. Some of this tissue is the persisting intima, another, the more important, the altered adventitia. Patches of granular and fatty tunica media may be seen in the vessel, just where the dilatation begins or where it is slight, but in most parts it has almost entirely disappeared. In some cases the wall of the aneurism is calcified.

Cylindrical and fusiform aneurisms are rounded or elongated symmetrical dilatations of the vessel. They occur in atheroma and arteritis, affecting the whole wall of the vessel for a shorter or longer distance. This condition is accompanied by (1) flattening of the intima, (2) thinning of the media, and (3) distension of the adventitia, the last-named coat forming the chief part of the wall of the aneurismal sac.

Sacculated aneurism is a unilateral dilatation of the wall of the vessel, the opening usually being smaller than the cavity into which it opens. The muscular coat disappears from the wall, the intima appears as a modified flattened coat, and the adventitia, which is composed of thickened fibrous laminae, between which are flattened connective tissue cells, forms the principal part of the wall of the aneurism, which in turn is usually lined by, or filled with, a laminated clot. This frequently occurs as a result of localised endarteritis in the second part of the arch of the aorta, at points where the large branches are given off from it or along their course, especially at the point where the celiac axis or other large branches are given off from the abdominal aorta, in the popliteal vessels, etc.

A *dissecting aneurism* is the aneurism formed when blood, escaping

through a weakened and ruptured intima, makes its way between the layers of the tunica media. The escaped blood may pass for some distance dissecting or separating the coats of the vessel, and then again make its way into the lumen. Such an aneurism may follow a fusiform dilatation, or it may be found where there has been chronic inflammation of the wall of the vessel, especially of the intima; it comes on very suddenly, and is due in most cases to the rupture of the brittle intima.

A *saddle-clot aneurism* is a sacculated aneurism, developed at the bifurcation of a vessel. It is usually due to the endarteritis, and consequent weakening of the wall, set up by an embolus arrested at the point of bifurcation of the vessel.

Miliary aneurisms, multiple sacculated aneurisms, occur in the brain as a result either of fatty degeneration or of periarteritis at many points in the small cerebral arteriole, the coats of the vessels being weakened and giving way at these points (§ 275).

FALSE ANEURISMS

277. A false aneurism is a cavity formed in connection with a vessel. This cavity, however, is not bounded entirely by the coats of the vessel; it may communicate with some other cavity, or its walls may be formed by the surrounding extra-vascular tissues.

A *traumatic aneurism* is formed where a vessel is wounded and the blood escaping into the tissues around the vessel, gradually displaces them until they form a limiting wall. If the wound in the vessel wall be large, there may be pulsation in a cavity so formed. A true aneurism may, by rupturing, form a false aneurism, the blood then escaping into and distending the surrounding tissues until a false aneurismal cavity is formed outside the true aneurism.

Varicose aneurism results from the opening of a true aneurism into a vein, or from false aneurism communicating with a vein. When venesection was more frequently practised varicose aneurism was especially common at the front of the arm in the bend of the elbow.

Aneurismal varix is a false aneurism of which the sac is formed by the wall of a vein. There is a direct communication between the vein and the artery, and whilst the latter remains comparatively undilated, the vein becomes enormously distended, in consequence of the direct

throwing in of the arterial blood and the resulting increase in the intravenous pressure ; in time its walls become thickened.

Other conditions which simulate aneurism, but which do not come under either of the above headings, are—

(1) The *cirsoid aneurism*, which consists of a number of small arteries, capillaries, and even veins, which are elongated, dilated, and frequently varicose. The whole mass of vessels forms a pulsating tumour, usually occurring on the face or head.

(2) *Aneurism by anastomosis*, where, along with enlargement of existing arteries, new arteries are formed, and a pulsating tumour is the result, also most frequently met with on the head.

DISEASES OF VEINS—PHLEBITIS

278. The commonest diseases of the veins are those met with as the result of inflammation. In acute phlebitis we may have the walls infiltrated with cellular tissue, with small granulations in the intima, and eventually thrombosis ; in the whole of this new tissue organisation takes place ; or, in consequence of the nature of the irritant (micro-organisms) which sets up these changes, the tissues may suppurate and we have what is known as suppurative phlebitis. (See Formation of Abscess, § 228 *et seq.*)

VARIX

279. In varix the superficial veins, especially those of the lower extremities and of the mucous membranes, become distended and tortuous. Irregular dilatations, or ampullæ, occur along their course, whilst here and there calcification of the wall takes place. On slitting open such a vein, the valves are found to be obliterated by the stretching of the intima, the valvular folds being drawn out. Surrounding the tortuous and dilated veins is, usually, a dense mass of connective tissue, which mats the vessels together. Harden (§ 62 or 63), stain (§§ 103 or 110 (*b*) and 132), and mount (§§ 193 and 199).

($\times 50$).—The inner coat is composed of laminated tissue, almost identical in structure with that described in endarteritis deformans. The longitudinal and transverse bands of muscle fibre are increased in size and number, being irregularly distributed in the thickened connective tissue. Here there is evidently actual hypertrophy of the muscular coat of the vein. The bands of muscle, stained yellowish-

brown, are surrounded by pink connective tissue, often containing golden-brown altered blood pigment. The adventitia is also somewhat thickened, and in it are numerous small blood vessels surrounded by collections of leucocytes and new connective tissue cells. Where the dilatation is very great and irregular, the muscular bands may

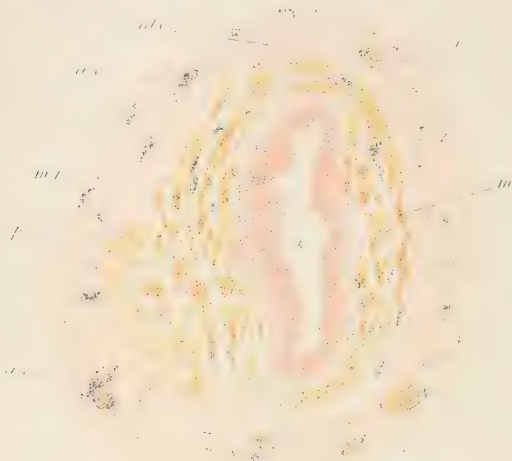


FIG. 96.—Section of varicose vein of the leg. Stained with alum haematein and van Gieson's stain. ($\times 20$.)

- adv.* Thickened and fibrous tunica adventitia in which the vasa vasorum (*a.v.*, *a.v.*) are surrounded by nuclei of migrating and proliferating cells.
- m.* Somewhat thickened muscular coat, at certain points (*m.f.*) broken into fragments or separated into layers by invading bands of new fibro-cellular tissue.
- p.* Altered blood pigment.
- i.* Irregularly thickened tunica intima.

have entirely disappeared at the points of dilatation, or they can be seen as granular or fatty masses scattered throughout the laminated connective tissue.

($\times 300$).—The above appearances must be verified.

Organisation in clot in veins takes place in the same manner as in arteries and in healing wounds or on serous surfaces (§§ 221–225).

CHAPTER VII

THE KIDNEY

280. The normal kidney is "smooth, and of a deep red colour." It weighs about $4\frac{1}{4}$ to $5\frac{1}{4}$ oz. (120 to 150 grms.) (§ 19); is about 4 inches long, $2\frac{1}{2}$ inches broad, and $1\frac{1}{4}$ inch thick ($10 \times 6 \times 3$ cm.), though the left kidney is somewhat longer and narrower than the right, and is also rather heavier. On close examination of the surface of the organ, small injected stellate veins are seen beneath the capsule. Make a longitudinal incision from the convex border to the hilus, then lay hold of the capsule with the forefinger and thumb and detach it. In a normal kidney this is readily done; the smooth surface is then seen to have a homogeneous or *slightly* mottled appearance, the stellate veins standing out prominently. On examination of the section, the kidney is seen to consist of (1) the cortex, forming the outer layer of tissue; (2) the medulla, or the part between the cortex and the pelvis; and (3) the pelvis, or funnel-shaped collecting basin into which, drained by the ureter, the papillæ converge. (For relative thickness of cortex and medulla, see § 19.) Radiating from the medulla to the cortical surface are numerous sets of parallel straight lines, which on close examination are found to be small arterial trunks; on each side of these are arranged, very regularly, a number of dark red, small, round, shining, almost translucent, points—the Malpighian bodies. Between them are opaque conical bundles of straight tubules. The straight tubules are longest midway between the double rows of Malpighian bodies, and reach nearly to the cortical surface, but nearer the Malpighian bodies they are considerably shorter. This structure will be examined more in detail under the microscope. On each side of the bundle of straight tubules is a somewhat irregular tissue, composed of sections of convoluted tubules. At the line where the cortical substance joins the medulla are numerous sections of vessels of considerable size, from which branches pass both upwards and downwards.

The medullary portion of the kidney is, for the sake of convenience, divided into two layers, the boundary layer, or that nearer the cortex, and the papillary portion, or that near the apices of the pyramids, dipping down into the pelvis. The pyramids of Malpighi, of which



FIG. 97.—Section of a small normal kidney injected with carmine gelatine.

- a.* Cortex; *h.* "superficial" cortex; *i.* interpyramidal cortex.
- b.* Medulla; *e.* boundary layer; *f.* papillary portion, with a chink where it opens into a calyx of the pelvis of the kidney—the only part of the calyx seen in the section.
- c.* and *c'.* Lines of interlobular arteries, with rows of Malpighian bodies—red dots—on each side.
- d.* Arteries of supply in boundary area.
- g.* Comparatively non-vascular part of the medulla.
- h.* Straight vessels. The relative vascularity of the cortex and medulla is well seen.

about eight are usually seen in the section, extend as inverted cones from the papillary portion, dipping into the pelvis, up to the superficial cortex (or that which does not dip down between the pyramids), and, between the bases of these pyramids, the cortex dips down for some

distance, forming the so-called interpyramidal cortex. The pyramids are made up of a series of alternating light and dark lines; the light lines are the urinary tubes which are continuous with the conical bundles of tubules in the cortex, and the dark lines the straight vessels, proceeding from the boundary area to the apices of the papillæ.

The papillary portion of the pyramid is considerably lighter in colour than the cortex, which is described as being "light crimson brown"; it is striated, the striæ being regular, and at right angles to the orifices of the papillæ as they open into the calyces or subdivisions of the pelvis. Much is to be learned from a naked-eye examination of the kidney, which should always be most systematically carried out.

For the pathologist, the kidney may be described as consisting of a series of lobules, and any change which is found in one of these lobules may confidently be looked for in any other. But before describing the lobule, one should have some idea of the various structures of which it is composed. These are—(1) The blood vessels; (2) the secreting urinary tubules; (3) the collecting urinary tubules; and (4) the connective tissue framework (§ 290).

281. *Blood vessels.*—The renal artery breaks up into a number of branches which, running in the submucous tissue from the pelvis along the sides of the Malpighian pyramids, enter the substance of the kidney at the boundary layer, at once breaking up into a number of arches, the convex surfaces of which are towards the cortex; from these arches in the boundary layer two sets of vessels pass, one upwards, the interlobular arteries, and one downwards, the straight branches which subdivide to form the arteriolæ rectæ. The interlobular arteries give off a series of lateral branches (afferent arterioles) almost at right angles, each of which passes to a Malpighian body, where it breaks up into a tuft of small capillary vessels—the glomerular tuft. These are again collected into a single vessel, the efferent arteriole, which carries the blood from the Malpighian body and then breaks up to form a network of capillaries; these capillaries surround the various tubules, and afterwards open into veins, which gradually unite to form the interlobular vein. In addition to the above branches of the artery and vein, there are interstitial and capsular branches to the connective tissue and capsule of the organ, and the interlobular vein commencing as the stellate vein already mentioned.

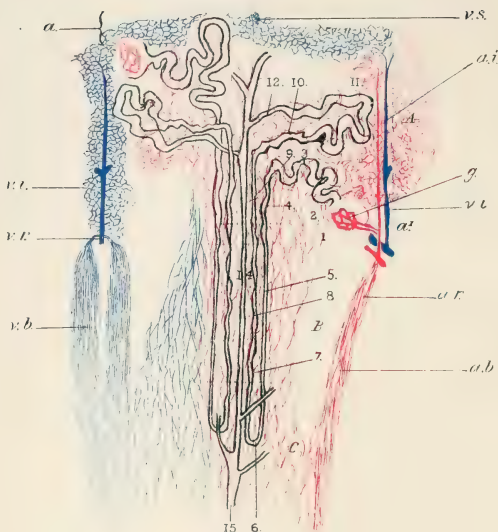


FIG. 98.—Diagram showing the course of the renal tubules, the arrangement of the vessels, and the Malpighian bodies. (Modified from Klein and Noble Smith.)

v.s. Stellate vein.

v.i. Interlobular vein.

a.i. Interlobular artery.

g. Glomerulus of Malpighian corpuscle.

a.r. Arteria recta.

v.r. Vena recta.

a.b. Bundle of arteriolæ rectæ.

v.b. Bundle of venæ rectæ.

A. Cortex.

a. Subcapsular layer, not containing Malpighian corpuscles.

a'. Inner layer of cortex, not containing Malpighian corpuscles.

B. Boundary layer.

C. Papillary part.

1. Bowman's capsule.

2. Neck at commencement of tubule.

3. Proximal convoluted tubule.

4. Spiral tubule.

5. Descending limb of looped tubule of Henle.

6. The loop.

7. Ascending limb.

8. Spiral part of ascending limb.

9. Narrow part in medullary ray.

10. The irregular tubule.

11. Distal convoluted tubule.

12. Curved collecting tubule.

13, 14, 15. Straight collecting tubule.

It is necessary to remember this arrangement of the veins in connection with chronic venous congestion of the kidney.

Passing downwards into the medulla from the arches in the boundary layer are numerous short vessels, which speedily break up, each one into a tuft or pencil of small straight vessels, the arteriolæ rectæ; these form a network with elongated meshes around the bundles of urinary tubules; they pass down as far as the papillæ. Beginning at the apices of the papillæ are small veins which return to the boundary layer, and take a similar course to the arteriolæ rectæ, around the bundles of straight tubules; in the boundary layer the blood from these meets the blood from the interlobular veins, and is carried away from the kidney by large venous trunks running in the submucous tissue to the hilus, and thence by the renal vein.

282. *Urinary tubules.*—These form the parenchyma, or substance proper of the kidney. Klein describes them as commencing “with a cæcal extremity in the Malpighian corpuscles,” and terminating “with an opening on the free surface of the papilla.” He then describes the tubules as composed of sixteen different segments, the first of which—(1) the Malpighian corpuscle, is in reality the invaginated and distended end of the blind tube (like the finger-tip of a glove turned inwards). Pushed into the invagination is a tuft of capillary vessels communicating on the one hand with the afferent arteriole, and on the other with the efferent arteriole, both of which pass into the involuted “tip.” The outer coat of the double covering of the capillary tuft is known as Bowman’s capsule. It is composed of a basement membrane, bounded on its external surface by connective tissue (which plays a most important part in certain pathological processes), whilst internally it has a layer of flattened endothelioid cells. Continuous with this layer of Bowman’s capsule is a similar layer of flattened cells covering the tuft of capillaries, forming what is in fact a reflection of the capsule. Supporting the capillary vessels is a delicate connective tissue framework (also very important), the nuclei of the cells of which are easily distinguished in stained specimens. Between the tuft of capillaries and Bowman’s capsule is a space which communicates by (2) a narrow opening, or neck, with the tubule proper. The tubule throughout its whole length is composed of a basement membrane, resting on which is a layer of epithelial cells. These epithelial cells vary considerably in both form

and structure in the different sections of the tubule. In the neck of the tubule they are almost cubical, but those nearest the glomerulus are flattened. Immediately following the neck, and therefore still near the Malpighian body, comes (3) the first part of the convoluted tubule, which, with the following part, (4) the spiral tubule, runs entirely in the cortex. In these the epithelium is columnar but somewhat irregular, especially in the spiral tubule, and each cell has a rounded



FIG. 99.—Malpighian body, and part of a convoluted tubule of the kidney of a dog. ($\times 100$.)

- a.* Capillaries of the glomerular tuft arranged in lobules.
- b.* Flat epithelial cells lining Bowman's capsule, and *b'*. similar cells covering the glomerulus.
- s.* Stalk of the glomerulus, composed of afferent and efferent arterioles.
- r.* The point at which the reflection of the outer lining layer of endothelium is reflected over the capillary tuft forming an investing layer for the capillary tuft.
- n.* Neck of the Malpighian corpuscle.
- c.* Longitudinal section of the first part of the convoluted tubule.

nucleus situated in its centre. The upper part of the cell, that near the lumen, is finely granular, but the part between the nucleus and the basement membrane is distinctly striated, the striae running longitudinally from the base of the cell to the nucleus. The next part of the tubule (the looped tubule of Henle) is principally within the medulla. The descending limb and the loop itself, (5) and (6), are lined by a layer of flattened epithelial cells. After the loop the ascending limb of the tubule (7) is lined with a layer of columnar

cells, each of which has its nucleus placed near the lumen. Passing further upwards (8) the lumen becomes narrowed, but the epithelium remains columnar. In the cortex (9) the ascending tube is narrower, and its epithelium more cubical or flattened. Still in the cortex is (10) the irregular tubule, lined by columnar cells, which vary very much in height, always, however, leaving the lumen of this part of the



FIG. 100.—Looped tubules of Henle cut longitudinally in both the boundary layer and the papillary portion of the pyramid. ($\times 100$.)

- a.* First part of the ascending limb of the looped tubule of Henle, in which the epithelium is columnar.
- b.* Part of the ascending limb.
- c.* The bend.
- d.* The descending limb and loop of the looped tubule of Henle, in all of which the epithelium is flattened and squamous. The tubules at these points are very like young blood vessels in appearance.

tubule very narrow. Then follows (11) the second or distal convoluted tubule, which is "identical" in position and structure with the first part of the convoluted tubule. After this, still in the cortex, are (12) the curved parts of the collecting tubule, and (13) part of the straight tubule, the lining of which is an irregular epithelium, with some of the cells cubical, others spindle-shaped, but all having well-marked

nuclei. Lower down in the medulla (14) the lumen of the tube is larger and the cells are cubical or slightly columnar, and each contains a spherical nucleus. (15) The lower parts of the collecting tubule, and (16) the large papillary duct are lined by epithelium of a cubical type, leaving a lumen of considerable size.

From the accompanying diagram and description it will be seen that, the straight collecting tube being taken as a central point, the looped tubules of Henle are arranged on each side, whilst further out come the sections of the two convoluted tubules, and lastly the Malpighian bodies at the ends of the afferent vessels which spring from the interlobular arteries. A lobule of the kidney is composed of the tissues between the interlobular arteries, and the prolongations of these tissues as they run down into the medulla.

In the cortex the lobule of the kidney may, like the lobule of the liver, be divided into three zones—peripheral, intermediate, and central. In the peripheral zone are the Malpighian bodies, with regular sections of the convoluted tubules. The intermediate zone, much narrower, is made up of the irregular and spiral portions of the convoluted tubules, the central zone containing the straight tubules and the larger collecting tubules.

The central zone only is continued into the medulla, where it is composed, as in the cortex, of the straight tubules of the descending limbs of the looped tubule, and of the straight collecting tubules. In the greater part of the papillary portion of the medulla the lobule is represented by the collecting tubes alone.

283. Examine a section of the cortex of an injected kidney (§ 49) made parallel to the convex outer surface.

($\times 50$).—A number of polygonal areas may be observed, each bounded by vessels, with here and there Malpighian bodies, in which the capillaries are injected. Within this vascular ring are numerous sections of tubules, some of them cut obliquely, others more transversely. Note that the lumen of each tubule is small and irregular; the epithelium is columnar, and each cell has a rounded nucleus near the lumen; the vascular meshes around these tubules are of considerable size. Nearer the centre are the tubules described as making up the intermediate zone, and here the loops of vessels are smaller, as not only are the tubules smaller, but they are more regularly cut transversely; the cells are more cubical, and the lumen is still narrow. In

the central zone the meshes of the network of vessels are again somewhat larger, as also are the openings in the tubules, the epithelium being cubical and occupying less of the tubule.

($\times 50$).—Examine a section cut at right angles to the above (the plane in which sections of the kidney are usually made). The zones of the lobules, as above described, can be made out in both the cortex

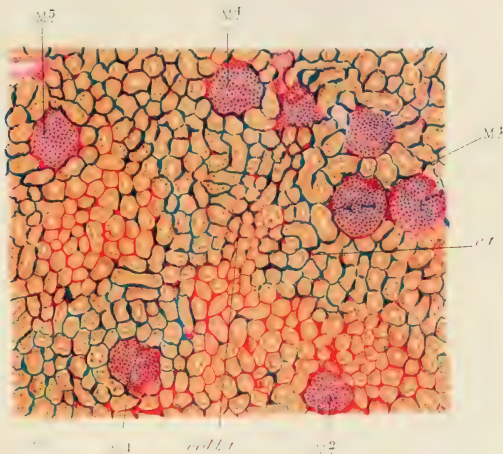


FIG. 101.—Section of normal kidney—transverse, *i.e.* made parallel to the convex surface of the organ and at right angles to the axis of the collecting tubules. ($\times 50$.) Injected with carmine and Prussian-blue and stained with alum hæmatein and picro-erythrosin. This shows the arrangement of the tubules, etc., in a “lobule.” Imaginary lines drawn between the Malpighian bodies M^1 , M^2 , etc., to M^5 mark the outlines of the lobule.

c.t. Convoluted tubules at the margin of the lobule.

coll.t. Group of small collecting tubules in the centre of the lobule.

Between these we have the various intermediary tubules.

and the medulla. Notice especially the large vascular meshes around the convoluted tubules in the peripheral and intermediate zones, the more elongated meshes around the straight tubules (seen now in longitudinal section) of the central zone. In the medulla, the long vascular bundles and meshes run down, between, and around the bundles of straight tubules.

($\times 300$).—Examine the arrangement of the tubules with their contained epithelium, the structure of the Malpighian bodies, the amount of

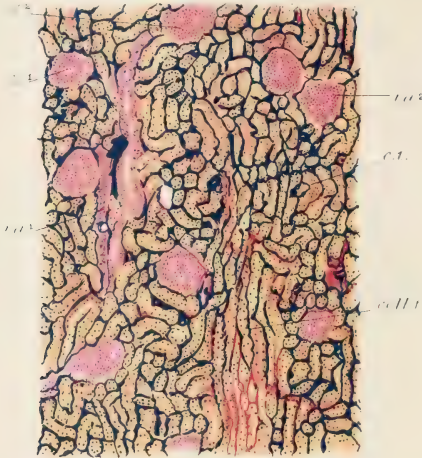


FIG. 102.—Section of a normal kidney parallel to the interlobular arteries and the long axis of the collecting tubules. ($\times 50$.) Injected with carmine and Prussian-blue and stained with alum hæmatein and picroerythrosin.

*i.a.*¹. and *i.a.*². Interlobular arteries between which lies the “lobule.”

*M*¹. Malpighian body on one side of this vessel.

*M*². Malpighian body on the opposite side of this vessel.

c.t. Convolute tubule at the margin of the lobule.

coll.t. Group of collecting tubules in the centre of the lobule.

connective tissue around the capillary loops of the glomerulus, around the glomerulus itself, around the tubules, and around the vessels.

TUBE CASTS

284. In our examination of the kidneys, various forms of casts and cysts will be met with, and in order that the student may understand something of them, it may be well to consider these intratubular formations somewhat systematically before we take up the principal diseases in which they occur.

Casts may be divided into four groups—(1) those derived from

the blood, following hæmorrhages into the glomeruli or tubules; (2) those composed of altered epithelium; (3) those formed of urinary secretions; (4) those made up of other materials not normally found in the tubules.

(1) *Casts derived from blood*.—Under the first heading come the various *blood casts* which are met with in acute nephritis—especially the scarlatinal form—in chronic venous congestion, or in acute congestion of the kidney. In the acute diseases they are most frequently composed of but slightly altered red blood corpuscles, and are commonly met with in the first part of the convoluted tubule. In the more chronic forms of disease they may be met with in the same position, but they are also seen as pigment casts in the lower parts of the tubules, where they may be golden-brown in colour, in which case they are composed of hæmatoidin crystals or granules; in the straight tubules they usually occur in the form of extremely black material, or melanin. In either case they are derived from blood which has escaped from ruptured glomerular, or less frequently, intertubular capillaries.

Hyaline fibrinous casts occur especially in acute inflammatory conditions, but they may be met with in healthy kidneys. They are usually seen in the looped and collecting tubules as delicate homogeneous casts filling a considerable length of the tube. They are extremely difficult to recognise in an unstained specimen, but may be seen as very delicately stained homogeneous masses in carmine (§ 106) or logwood (§ 108 *et seq.*) stained sections. They form the basis of a large number of other casts. We may find fibrinous lymph in the casts from cases of acute nephritis and even leucocytes, but more commonly the casts are quite homogeneous, and appear to consist of coagulated serum albumin, which has made its way from the glomerular capillaries into the tubules.

(2) *Casts derived from the renal epithelium*.—The most common of these is the *colloid* (or glue-like) *cast*, a homogeneous, yellowish, translucent mass, found especially in the lower parts of the convoluted tubules in almost all cases of kidney disease where there are marked epithelial changes, as in waxy kidney, and in subacute and chronic interstitial nephritis. In some cases there are retained in the casts the dim outlines of the cells of which they are composed, but usually they appear to be composed simply of a glue-like material, which gives a yellow reaction with picro-carmin (§ 102), a brown

reaction with iodine (§ 133), but a bluer purple with methylanilin-violet (§ 117) than is given with "waxy" material. They stain deeply with other reagents. They are usually surrounded by a layer of flattened epithelial cells, which appear to proliferate and add layer after layer of degenerated cells to the surface; consequently, the cast may in some cases present faint traces of lamination.

Granular casts are met with in the convoluted tubules in inflammatory conditions, or where marked atrophic changes are taking place in the epithelium. They have a hyaline centre surrounded by a granular protoplasmic outer layer, which appears to be derived from degenerating epithelial cells; these casts are larger than the ordinary hyaline cast. Some authors apply the term granular only to those casts that are derived from degenerated blood or to dissolved blood pigment which is deposited in the epithelium, and forms the basis of the brown granular tube casts.

Fatty or oily casts are hyaline casts on the surface of which are fatty or albuminoid globules, derived apparently from degenerating epithelial cells. (Not always fatty.)

Epithelial casts are usually found in the looped and straight tubules when these are in a condition of acute catarrh. Each has a hyaline basis, and is covered with a number of cells, derived either from the epithelium of the straight tubules or from extravasated leucocytes. Only those casts which are formed in the looped or straight collecting or excretory tubules come unchanged to the urine, but similar casts may be found in the upper parts of the tubules in sections of the kidney.

(3) *Casts formed from urinary salts, etc.*—As seen in the case of the granular contracted kidney, crystals of acid urate of soda accumulate in the tubules of all parts of the kidney, giving rise to the yellow patches mentioned under that disease.

Similar deposits of uric acid, or urate of ammonia or soda, are frequently met with in the excretory tubes near the apices of the papillæ in children who die within from two to fourteen days after birth, as "yellowish or brick-red lines," running from the apices for some distance towards the bases of the pyramids.

(4) *Casts of foreign material.*—*Bilirubin casts* are dark granular casts, occurring chiefly in the straight tubules during the course of long-continued jaundice. They are probably closely allied to blood casts.

Calcareous casts are met with in the straight tubules in aged people, and in cases of osteomalacia, where there is rapid absorption of the calcareous salts from bone. These salts are deposited as white masses in the looped tubules or in the excretory tubules near the apices of the papillae. "They consist of dark, strongly refractile globules or nodular masses, which join together to form nodular rods." In a second form there is "an albuminoid basis, infiltrated with carbonate of lime." These stain deeply, but irregularly. On the addition of a weak acid they disappear, and carbon dioxide is given off. They are composed principally of carbonate of lime.

CYSTS IN THE KIDNEY

285. *True secondary cysts* may be formed in one of three ways—

(1) By distension of Bowman's capsule of the Malpighian body, owing to the obstruction of the narrow outlet or neck, frequently by a plug of colloid material, or, more rarely, by constricting fibrous bands. These cysts are seldom of large size, as the outflow of the watery part of the secretion from the capillary tuft ceases as soon as the pressure in the cyst equals that in the blood vessels. The capillaries gradually atrophy when their function is interfered with, and a cyst is left. These may be filled with watery material, or with colloid material derived from the degenerating epithelial cells.

(2) Simple cysts in the tubules are formed in the same manner.

(3) Rows of cysts are formed where the convoluted or straight tubules become irregular, varicose, and tortuous, forming a chain of small cysts. They occur especially in the granular contracted kidney, and in the tubules which are situated near the margin of the wedge-shaped fibro-cellular mass, where the convoluted tubule is alternately outside and within the granular patch. Colloid plugs are formed at certain points, usually where there is already slight constriction from the pressure of fibrous bands: above this point there are other slight constrictions, and as the tube becomes distended it becomes so unequally—especially where it lies outside the solid area—and a row of cysts is formed, the dilatations and constrictions alternating.

For cysts to increase in size there must be two factors at work—

(1) the watery secretion must be going on above the constricted point: and (2) epithelium must be growing, must be shed, and then, under-

going degeneration, must be washed by the urine until it eventually forms colloid material.

The contents of these cysts may be—

- (1) Serum, or the watery constituents of the blood along with its salts. This is the most common form.
- (2) Colloid; a gelatinous, homogeneous material, derived from degenerated epithelium.
- (3) Urinous salts or urates.

Cysts are most frequently found in the granular contracted kidney, and in the various forms of interstitial nephritis.

Primary cysts.—These are found in the so-called cystic degeneration of the kidney. There are two forms—the congenital, and that which occurs during adult life.

In the first form, which occurs during foetal life, the kidney may be enormously increased in size, or it may be smaller than normal. Both organs are affected. The cysts, which form the greater part of the organ, are probably distended tubules and glomeruli, the secretions of which cannot escape, owing to constriction of the efferent tubes in the atrophied papillæ. These cysts, unlike the following form, contain urinary fluid and salts.

The second form is very frequently unsuspected during life, and usually gives rise to no symptoms until the patient is advanced in years. Both kidneys are enlarged, and are converted into numerous cysts, which vary very much in size, from that of a millet seed up to two-thirds of an inch, or even more, in diameter. They are filled with a fluid containing albumin and blood pigment in various stages of alteration, and present all shades of colour, from yellow, through green and blue, up to purple. Cholesterin crystals are also met with, and, in rare cases, oxalate of lime and leucin—rarely any urinary salts. The fibrous cyst walls “are partially lined with flattened polygonal cells.” It is quite possible that this may be the slowly growing or fully developed congenital form, but as yet little is known of the mode of development of either of the forms of cystic degeneration.

CHRONIC VENOUS CONGESTION OF THE KIDNEY

286. Synonyms, “Cyanotic” Kidney (not a good term), “Congestive Induration,” “Passive Hyperæmia” of the Kidney.

In chronic venous congestion of the kidney, we have distension and

thickening of the veins and venous capillaries with wasting of the parenchyma, brought about by pressure and malnutrition.

This condition is met with in conjunction with valvular disease of the heart, more especially with mitral disease, in chronic fibroid phthisis, chronic bronchitis, and emphysema; in fact, it occurs under just the same conditions as does chronic venous congestion of the liver (§ 238), to which it is analogous, and with which it is frequently associated.

In cases of heart disease, during the course of which albumin in the urine or slight hæmaturia has been present, this condition may very frequently be found after death.

Naked-eye appearances.—In the earlier stages of the congestion the kidney is enlarged; it may be as much as 7 or 8 oz. (200 to 225 grms.) in weight, and is firm and elastic. Under the capsule, the venæ stellatæ are considerably distended and are very prominent. On section the capsule is readily removed; the cortex is smooth, markedly congested, and has at first a deep purple colour, which rapidly turns to crimson.

On examining the section of the cortex more carefully, its thickness is seen to be slightly increased, the Malpighian bodies stand out as red dots, arranged regularly in parallel rows on each side of the prominent interlobular vessels (distended interlobular veins). The most marked changes, however, are in the medulla, where the venulæ rectæ stand out prominently, especially near the bases of the pyramids, which are deeply congested; the tissue has a distinctly striated appearance, the congested vessels shining out very prominently between the bundles of uriniferous tubules. In old-standing congestion, irregular pale patches (due to fatty degeneration of the epithelium in the tubules) may make their appearance, and the organ may be diminished in size and feels almost fibroid.

Harden (§ 62 or 63), cut (§ 82 *et seq.*), and stain (§§ 102, 103, or 104, or 110^b and 132). The following description applies to the later stages of the disease: in the earlier stages we see simply the distension of the vessels without any of the structural changes.

($\times 50$).—The interlobular veins in the cortex are filled with coloured blood corpuscles. Following the course of these veins, it is seen that the capillary plexus between the convoluted and straight tubules, the afferent arterioles and the glomerular capillaries, are all distended with the same corpuscles. The glomeruli are, in some

cases, very much increased in size, and the connective tissue nuclei may be increased in number. In the medulla the straight vessels are extremely prominent, being all distended with coloured blood corpuscles.

Next examine the tubules. The capillaries in the Malpighian

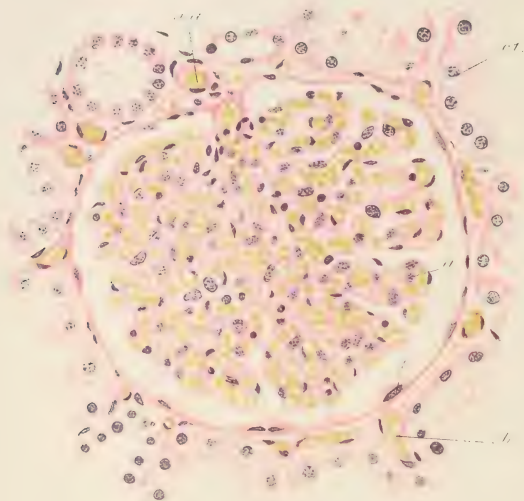


FIG. 103.—Drawing of a section of the cortex of a kidney in a state of chronic venous congestion. Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Capillaries of glomerular tuft distended with blood.
- b.* Intertubular capillaries in a similar condition.
- a.a.* Afferent arteriole seen in transverse section.
- c.t.* Convoluted tubules.
- e.* Flattened cells lining Bowman's capsule.

It will be noticed that there appears to be a considerable thickening of the walls of the vessels between the sections of the convoluted tubules.

bodies often show signs of rupture, small extravasations of blood are found within the glomerular capsule, and large masses of altered blood may be seen in the convoluted tubules. In the straight tubules in the medulla small collections of golden-brown pigment (derived from the blood) are met with, and here and there almost inky black "melanin"

casts occupy a few of the tubules in the papillary portion of the medulla. The epithelium may be granular, with small globules of fat in the protoplasm of the cells, which in some cases nearly fill the tubules. Very frequently there are wedge-shaped patches of fibro-cellular tissue under the capsule, the base of the wedge being near the surface, the apex extending for some little distance into the cortex; these patches extend along the lines of the interlobular vessels, and enclose some of the Malpighian bodies, which then become atrophied

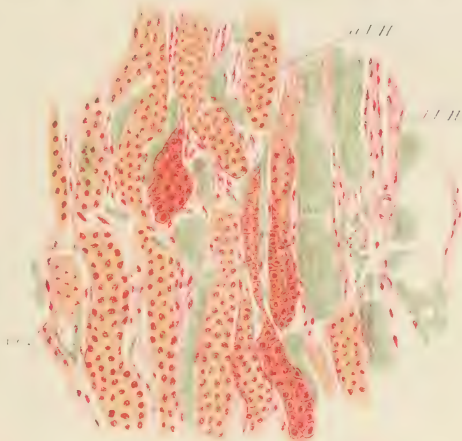


FIG. 104.—Drawing of a section of a kidney (boundary layer) in a state of chronic venous congestion. Stained with picro-carmin. ($\times 300$.)

v.c. Vessels distended with coloured blood corpuscles.

a.l.H. Ascending limb of looped tubule of Henle. Spiral portion and collecting tubule.

d.l.H. Descending limb.

and fibroid. The tubules involved in these masses are atrophied and small, and their epithelium is flattened. This is said to be the result of an intercurrent inflammatory condition, but it is one which is frequently met with in this disease.

($\times 300$).—The capillary tufts in the Malpighian bodies are greatly enlarged, the vessels being distended with red blood corpuscles; between the tuft and Bowman's capsule, blood corpuscles in various stages of disintegration may sometimes be seen. Frequently there

appears to be a slight increase, not only in the number of connective tissue nuclei, but also of the fibrillated tissue around the walls of the capillaries. In the convoluted tubules the epithelium is comparatively healthy, though in some cases it is in a condition of cloudy swelling, or even fatty degeneration. In the lumina of these tubules small collections of broken-down blood corpuscles, or of golden-brown pigment derived from the small hæmorrhages within Bowman's capsule, are often seen. The vessels between the tubules are greatly distended; their walls are thickened, and take on a pink reaction with carmine, just as in the case of the thickened hyaline-looking vessels seen in "Nutmeg Liver" (§ 238). In the medulla the longitudinal and transverse sections of the straight vessels are filled with blood, the walls are thickened, and are stained pink. In the tubules the epithelial cells may be undergoing degenerative or proliferative changes. There may be fatty globules in the cells. Here, too, are found the "melanin" casts already referred to as composed of the altered blood pigment.

The wedge-shaped patches in the cortex consist of pink fibrous tissue, with a few round cells at the margin. The Malpighian bodies in them are atrophied and fibrous looking (§ 298 *et seq.*), whilst the enclosed tubules are small, and the epithelial cells lining them are flattened, extremely granular, and atrophied, some containing small globules of fat, which stain black with osmic acid. The study of these sections will give an exceedingly good idea of the vascular supply of the kidney.

The above, mostly mechanical, changes are first seen in the veins—the stellate, interlobular, and straight medullary veins being first affected—then in the capillaries, and lastly in the arteries. Distension and thickening of these take place as in "nutmeg" liver. The changes in the epithelium are seen only in the later stages, and are due, in great measure, to pressure and malnutrition. The general increase in the amount of connective interstitial tissue is sometimes marked, and appears to result directly from the venous congestion corresponding to the increased growth of bone associated with the same condition.

FAT EMBOLISM OF THE KIDNEY

287. Fat embolism is met with in certain cases of diabetic coma, or in the similar coma following fracture of bones, especially of the bones

of the head and of cancellous tissue in the "short" bones, or at the ends of "long" bones, and when these fractures are accompanied by septic mischief. In both these conditions fat is set free to circulate in the blood, and is eventually arrested in some of the smaller vessels.

The naked-eye appearances vary considerably, but the points to be specially looked for are pallor, increased size, and flabbiness of the organ, and minute hæmorrhages under the capsule or on the surface of the sections.

Where fat embolism is suspected, make a microscopic examination in the fresh condition. To make a more exhaustive examination harden (§ 62 or 63), and stain a section first with osmic acid (§ 135) and then (§ 102 or 103).

($\times 50$).—There is evidently some congestion, especially at certain points near the surface of the cortex. Near the congested areas, filling some of the vessels between the tubules, black masses, evidently fat stained with osmic acid, are seen. Similar black emboli are also seen in some of the capillaries in the glomerular tuft, and in the straight vessels. Near these congested areas are small hæmorrhages along with which some of the fatty material may have escaped into the surrounding tissues, or even into the tubules, especially where rupture of the capillaries in the Malpighian tuft has occurred.

($\times 300$).—Verify these appearances, special care being taken to localise the fat in the positions above mentioned.

WAXY OR LARDACEOUS DISEASE OF THE KIDNEY

288. This disease is frequently associated with other marked changes of the tubules and of the interstitial tissue, as in syphilis, but as these are rather superadded conditions, it will be well to confine the description to the waxy change, and take up the other conditions separately. For example, waxy disease is frequently associated with interstitial nephritis, in which case the changes due to the waxy condition are to a certain extent masked by those due to the interstitial processes. For conditions under which this disease occurs, see § 237.

Naked-eye appearances in the early stage. The kidney is usually slightly enlarged, and the capsule strips off very readily; the surface is smooth, glistening, anæmic, and often yellow.

On section the cortex is pale and anæmic, and the Malpighian

bodies are seen as glistening rounded masses, arranged regularly in parallel rows; the surrounding tubular tissue has a peculiar

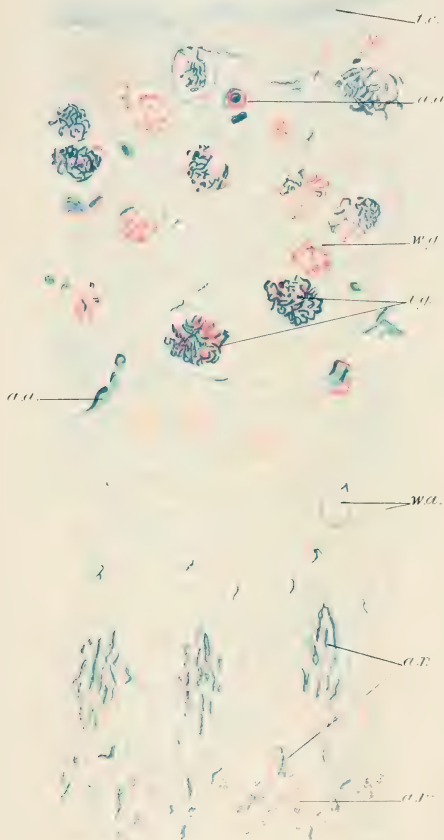


FIG. 105.—Drawing of a section of a waxy kidney, injected with soluble Prussian-blue. Stained with methylanilin-violet, and treated with oxalic acid. ($\times 50$.)

t.c. Thickened capsule, underneath which new interstitial tissue may be seen.

w.g. Malpighian tuft, completely waxy, through which the injection has not passed.

i.g. Tuft, in which capillaries are not so much affected, the injection passing into most of them.

a.a. Afferent vessels, waxy.

w.a. Larger artery in boundary area, and, *a.r.*, *a.r.*, arterioles seen in both longitudinal and transverse section, all waxy.

The small inter-tubular waxy capillaries are seen as delicate red violet streaks throughout the section.

mottled look, though there are no very marked evidences of fatty degeneration.

In the medulla the appearances are also very characteristic. The striation at the base of the pyramid is slightly exaggerated, the congested straight vessels standing out prominently from the pale tubules, and there is usually, even in this early stage, a comparatively deep colour, due to congestion; the apices of the papillæ remain pale.

Pour iodine (§ 133) over the fresh surface of the section, and note that dark mahogany lines make their appearance in the position of the straight vessels, and that the glassy-looking Malpighian bodies also take on a brown stain. In an earlier stage, where otherwise no naked-eye changes are distinguishable, the iodine staining frequently brings out the fact that there is slight waxy degeneration in patches in the Malpighian bodies and in the walls of the straight vessels.

Harden (§ 58, 60, or 63) and mount one section unstained (§ 195). Stain others (§§ 103, 117, and 133).

($\times 50$).—In the unstained specimen the Malpighian bodies are enlarged and translucent. This translucence does not extend throughout the whole of the capillary tuft, certain of the capillary vessels only being affected. Their walls are thickened, homogeneous, and glassy, and have a yellow tinge; the transverse diameter of the vessel as a whole is increased. Parts of the tuft remain perfectly healthy, so that there is a kind of picking out of the tuft with the waxy material. The afferent arteriole is also affected, small areas of the middle coat being quite glassy looking; in the medulla the arteriolæ rectæ are undergoing similar changes.

In the iodine-stained section the waxy areas are seen as mahogany brown patches when examined by reflected light, whilst the normal tissues appear yellow; with methylanilin-violet the waxy parts, seen by transmitted light, stain *red* violet, whilst the normal tissues and fattily degenerated cells take on a *blue* violet or slate-blue colour. At this early stage the changes in the epithelium lining the tubule are comparatively slight, but in the advanced stage they are far more marked. Colloid casts may be found even in this early stage. They are perfectly homogeneous, and fill up the lumen of the tubule, whilst the epithelium around them is usually considerably flattened. Such a cast, unstained or stained with iodine, is very like waxy material, but, stained with methylanilin-violet, it gives an intermediate colour between the *blue* violet of normal tissues and the *red* violet waxy reaction.

($\times 300$).—Note the patches of waxy material in the walls of the capillaries of the glomeruli, and that the flattened cells and the base-

ment membrane of Bowman's capsule are unaffected. In the muscular coat of the afferent arteriole observe the swollen and translucent (or red violet) patches; and that the diameter of the whole vessel is increased, although the lumen is greatly diminished in size. Note, too, the marked changes in the arteriolæ rectæ, and that the vessels near the papillæ are more affected than are those near the base of the pyramid. If this be remembered when the naked-eye examina-

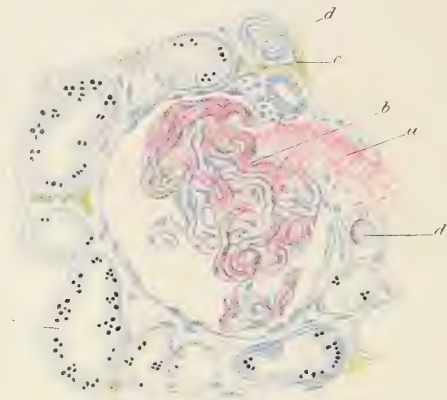


FIG. 106.—Section of waxy and fatty kidney. Stained with methyl-anilin-violet and osmic acid. ($\times 350$.)

- a.* Afferent arteriole, waxy. Stained red violet.
- b.* Capillaries of Malpighian tuft, waxy in patches.
- c.* Waxy intertubular capillaries.
- d.* Colloid casts, stained intermediately between waxy and healthy tissues.
- e.* Fat granules and globules in epithelium, stained black with osmic acid; healthy tissues stained blue; red blood corpuscles unstained, seen as yellowish-green corpuscles in the capillaries.

tion is made, it will be readily understood why the base of the pyramid is almost invariably relatively deep in colour. The consequent diminution in the diameter of the vessels also suggests the cause of the pallor of the organ, even in the early stage. Further, not only is the quantity of blood passing through the organ lessened, but, from the nature of the causes of the disease, its quality is very much deteriorated. To these two factors the fatty changes which occur

during the later stages of the disease are also to be ascribed. The appearances of the colloid casts, as above described, must be verified under the high power, and the chemical and colour reactions again observed. The epithelium is usually comparatively healthy throughout, though slight fatty degeneration may be met with.

WAXY KIDNEY—MORE ADVANCED STAGE

289. In the later stages the kidney is very soft and flabby; it may be enormously enlarged, even to twice its usual size. The capsule strips off readily, the surface is smooth and pale, having a dull brown or brownish-yellow tinge as a groundwork, mottled with numerous paler patches. On section, the increase in size is seen to be due, in great measure, to the increase in the thickness of the cortex. The Malpighian bodies are enormously swollen, and stand out prominently as glistening masses of considerable size. With a hand-lens the vessels between the tubules are also seen to be glistening and swollen, whilst the tubules themselves are pale and fatty looking. The striation of the medullary rays is distinctly marked, and there is marked congestion at the bases of the pyramids, near the boundary layer. The tips of the papillæ are extremely pale. With a watery solution of iodine (§ 133), the mahogany brown staining is widely distributed. The Malpighian bodies, the interlobular arteries, the intertubular plexus, and the straight vessels in the medulla are all affected. Harden (§ 58, 60, or 63), examine one section unstained (§ 195), stain others (§§ 117 and 133).

($\times 50$).—The change is wide spread. In the Malpighian body the capillary tuft may be very extensively affected, the smaller waxy patches in the individual capillaries running together. In the basement membrane of Bowman's capsule there may be a similar waxy material. The interlobular and afferent arterioles are markedly affected, as are also the efferent arterioles, and, in a less degree, the intertubular capillary vessels. A similar change may be noted in the basement membrane of the convoluted tubules; waxy change in the epithelial cells is very rare indeed. In these cells, however, owing to malnutrition, fatty degeneration is of frequent occurrence, the cells becoming angular and shrivelled, and when treated with osmic acid (§ 135) numerous black globules and granules of fat are seen in them.

In the medulla, from the boundary layer to the apices of the papillæ, the waxy change is in the walls of the vessels and in the basement membrane of the straight tubules. It is always most marked in the muscular coat of the vessels; but in the later stages the intima may be involved, the endothelial lining in such cases undergoing fatty degeneration. Nearer the tips of the papillæ the



FIG. 107.—Section of medulla of waxy kidney. Stained with iodine and sulphuric acid. ($\times 310$. After Kyber.)

- a.* Straight tubule with colloid cast (*c.c.*) in its lumen.
- b.* Epithelium.
- d.* Shed epithelium, fatty and colloid.
- e.* Basement membrane; waxy (blue).
- f.* Descending limb of looped tubule of Henle. Waxy basement membrane. Cells fatty.
- g.* Vessel, the walls of which are in an advanced stage of waxy degeneration.

connective tissue fibrils between the bundles of muscle fibres, which, in the normal kidney, run from the tips of the papillæ for some distance towards the boundary layer, are affected, apparently quite apart from the vessels; this change may occur where the other tissue elements of the kidney are comparatively unaffected. The colloid casts are somewhat numerous throughout the whole

section; they have already been described in the earlier stage. True waxy casts are described as occurring in extremely advanced cases, but this must be a very rare condition.

Greenfield gives the order of affection of the various parts, by the waxy degeneration, as follows:—(1) Afferent arterioles; (2) groups of glomerular capillaries, especially those of the superficial cortex; (3) arteriolæ rectæ; (4) efferent arterioles, and the capillaries into which they break up; (5) capsule of Malpighian body; (6) the capillaries which run between the bundles of straight tubules; (7) the basement membrane of the convoluted tubules; (8) large interlobular arteries; (9) walls of the straight tubules, especially near the papillæ; (10) large branches of arteries and veins in the boundary area; (11) the connective tissue around the collecting tubules at the tips of the papillæ; and (12) the epithelial cells very rarely.

GENERAL TISSUE CHANGES IN BRIGHT'S DISEASE

290. In considering the following forms of kidney disease, it is essential that the changes which take place in the various tissues under different conditions, and that the interdependence of certain of the acute forms of Bright's disease and corresponding chronic forms, should be understood. Inflammation in the kidney differs in no respect from inflammation in any other organ, except in so far as the different arrangement of the tissues and the distinct function of the organ may lead to certain differences. Here changes are met with in the vessels, in the connective tissue, and in the epithelial lining of different tubes and cavities. The vascular and connective tissue changes present special features and induce distinct phenomena, because these tissues are arranged around the tubules, and in and around the Malpighian bodies. Further, the various epithelial changes have different characteristics, simply because the epithelium is divided into three groups, namely—(1) that covering the capillaries of the Malpighian tuft and lining Bowman's capsule of the glomerular body; (2) the secreting epithelium of the upper part of the urinary tract; and (3) the epithelium lining the excretory ducts.

Here, as in inflammatory diseases of the liver, although the nutrition of *all* the tissues is affected, the degree in which the different tissues suffer varies materially. It may be found, for example, that in one form the changes in the connective tissue predominate, and that

associated with them very slight alterations are met with in the secreting epithelium, though these always tend to become more marked as the disease progresses. On the other hand, the epithelium may undergo grave changes in cases in which it is difficult to make out any pronounced vascular or connective tissue lesions. Again, there may be marked affection of the tubular portions of the kidney, whilst the Malpighian bodies manifest little evidence of inflammatory reaction. Note, however, that the Malpighian bodies may be the seat of considerable alteration before the tubules beyond them give any very definite evidence of inflammatory disease, though such evidence invariably follows at a later stage.

With all this, it may be that the epithelium of the excretory tubules remains entirely unaffected; in fact, evidence of disease in the excretory tubules is of comparatively rare occurrence. It will be evident, then, that in making any examination of the kidney for inflammatory lesions, our attention should invariably be directed first to the secretory portion of the kidney, the cortex, as only in very rare cases is it found that the tissues in the bundles of straight tubules participate in the inflammatory changes; it must be borne in mind that the secretory portion of the kidney extends into what is spoken of as the interpyramidal cortex.

In consequence of the peculiar relation of the Malpighian body to the remainder of the tubule, we may have marked inflammatory changes in the tissues in and around the glomerulus, which lead to interference with the proper discharge of its functions; the tubules below are no longer called upon to perform their special functions, and they undergo atrophic changes. These atrophic changes may or may not be associated with inflammatory changes in and around the tubules; and, according as the inflammation is present or absent, very marked differences, to which reference will be made in the description of inflammatory forms of kidney disease, are found.

Briefly, the special conditions met with in inflammation are the following: first, those which occur around the vessels and in the connective tissue; secondly, those met with in the Malpighian body; and, thirdly, those that are found in the tubules.

In the interlobular arteries and in the afferent arterioles in acute septic conditions, bacteria may be found in small embolic masses; these may make their way into the surrounding connective tissue, and will be more fully described later. In certain forms of interstitial

nephritis, thickening of the intima leading to endarteritis obliterans (§ 273) may occur. Far more important, however, than these conditions is the hyaline swelling of the middle coat of the vessel (§ 269), and also, in certain cases, of the intima and even of the adventitia, which is probably due to an increased absorption of fluid by the elements of which the various coats of the vessel are composed. It occurs especially in the early stages of acute inflammatory disease, and may lead to considerable diminution in the size of the lumen of the vessel in which it takes place. It is almost invariably associated with the escape of leucocytes from the small vessels immediately behind it, and also with the proliferation of the fibroplastic cells in its neighbourhood.

In the glomeruli there are, as one would expect, several sets of changes, two or three of which, however, are usually associated. In certain cases, owing to slight hyaline thickening at the point of entrance of the afferent arteriole, there is slight constriction, followed by exudation of leucocytes; then, too, the connective tissue which surrounds or forms the outer part of the capsule may participate in the general connective tissue changes, as a result of which the glomerular capsule—Bowman's capsule—is distinctly thickened. In other cases the basement membrane may become swollen or thickened, or, as we have already seen (§ 288), it may undergo waxy degenerative change. The layer of epithelium lining the capsule may proliferate, and layer upon layer of cells being formed, they may ultimately assume an almost fibrous appearance, or they may become hyaline. Thickening of the capsule may from these several causes be so marked that the capsule and the vascular tuft are almost obliterated. Within the capsule albuminoid casts may be met with, or extravasations of blood (the result of hæmorrhage), or, in leucocythæmia, large numbers of leucocytes have escaped from the glomerular tufts, the blood in some cases becoming degenerated *in situ*, or, far more frequently, finding its way into the convoluted tubules, where it undergoes degenerative changes; the pigment is set free and is then taken up into the epithelial cells. The cells investing the capillary tuft may also undergo proliferation, fatty or more rapid degenerative changes, or may even be detached bodily. The connective tissue cells supporting the capillary network are sometimes seen to proliferate. Coming now to the capillaries themselves, we find that the endothelium may undergo fatty degeneration, the basement membrane may become

swollen, or it may undergo waxy degeneration, whilst, actually within the vessels, thrombi or emboli—simple, or containing micro-organisms—may sometimes be found.

The connective tissue must be looked upon as a kind of lymphatic sponge formed of a network of fibrils covered with flattened endothelial cells; through the lymph spaces so formed is a free circulation of fluid, in which float numerous lymph cells. In inflammation two sets of changes are set up in this connective tissue—(1) There is an escape of fluid lymph and polymorpho-nuclear leucocytes, and perhaps a number of lymphocytes, from the blood stream into the lymph spaces; when this becomes very great, a few red blood corpuscles may also escape, and in very acute cases the spaces may become distended with fibrinous lymph, which, clotting in them, gives rise to a very characteristic appearance. In most cases, however, the only evidence of inflammatory exudation is an increase in the number of round cells in the lymph spaces, and a swelling of the fibrils of which the connective tissue network is composed. (2) In more chronic cases there may be a proliferation of the endothelial cells covering the fibrils, as a result of which there is an increase in the amount of connective tissue between the tubules, just such as occurs in the healing of wounds or in common cirrhosis of the liver. Wherever this takes place, we may expect to find cicatrization, contraction of the fibrous tissue, and compression of the tubules leading to atrophy or to irregular dilatation.

In the tubules, as in other positions, the basement membrane may undergo hyaline or waxy change, and the epithelium may be affected by all kinds of degenerative changes. In the very early stages of inflammation the cells become swollen, they lose their normal shape, the striation at the base of the cell is lost (see § 282), the protoplasm becomes more coarsely granular, and the nucleus is less distinctly stained; this may become so marked that, ultimately, a great part of the cell is broken down, and the nuclei remain entirely unstained, clear spaces making their appearance in the degenerated protoplasm.

291. In certain acute forms of kidney disease, and even in sub-acute and chronic nephritis, what is known as “catarrh” frequently occurs—an active proliferation of the epithelial cells lining the tubules; as those cells near the lumen are formed as the result of fission, they are cast off and washed away by the urine. It will be noticed in

these cases that not only the cast-off cells, but also those that remain attached to the basement membrane, assume very irregular shapes, - some are pear-shaped, others globose, others flattened and spindle-shaped, and more like endothelial cells. This process of catarrh should be very carefully studied. Wherever there is catarrh there is usually fatty degeneration, though this latter condition may be present where there is no marked evidence of catarrhal change. In a section stained with osmic acid, small black globules and granules may be seen distributed throughout the protoplasm of the epithelial cells; but in all cases it will be observed, especially in the convoluted tubules, that the larger globules are usually situated near the base of the cell (see Fig. 110). Fatty degeneration, like catarrh, is usually met with in the upper part of the secreting tubules, the epithelium of the straight and excretory tubules, except in special diseases, being much more rarely affected; the same remark applies to the glycogen, which is sometimes seen in diabetic kidneys in which a number of clear globules, not reacting to osmic acid, but which give a distinct reaction with iodine, may be demonstrated in the epithelial cells. In the tubules, casts having a hyaline basis (probably serum albumin) are seen; around this hyaline basis are epithelial cells in various stages of degeneration, sometimes containing granules of blood or bile pigment. Blood corpuscles in various stages of degeneration, or masses of leucocytes, the result of acute inflammation or of leucocythæmia, may take the place of epithelial cells in these casts. The tubules may become distinctly atrophied, such atrophy being invariably associated with impairment or loss of function; this may be due to an altered blood supply and an increase of connective tissue around the tubule, in which case it may be spoken of as *primary* atrophy. When the loss of function is due to failure of the Malpighian body to separate the fluid elements of the blood, so that the tubule below has comparatively little work to do, the tubules become small and the epithelial lining shrivelled and atrophied. This may be looked upon as *secondary* atrophy, and is certainly quite distinct, both as to causation and course, from the primary atrophy above mentioned.

When it is remembered what part the kidneys play in the separation and excretion of effete and poisonous matter from the blood, it is readily understood how different parts of the organ may become affected. If a poisonous substance is rapidly excreted by the epithelium, it may, in its passage through the secreting cell, so

modify the structure, or so over-stimulate the protoplasm of the cell, that cloudy swelling or catarrh is rapidly and certainly developed, whilst the nutrition of the cell may be so interfered with that ultimately it undergoes fatty or other degenerative changes. If, on the other hand, any poisonous or irritant substance is poured out with the fluid elements of the blood from the capillaries of the glomerular tuft into Bowman's capsule, it will easily be understood how fibrin may make its way into that space, or how there may be proliferation of the cells around the vessels and lining the capsule. Returning to the vessels, constriction of the afferent vessel may lead to diminution in the size of the tuft, followed by a kind of compensatory thickening of the capsule—all this leading to the secondary atrophy of the convoluted tubule connected with the affected Malpighian body.

Lastly, should the connective tissue be specially involved, *i.e.* should the poisonous material circulate freely in the lymphatic system, and not pass at once into the secreting cells, a series of connective tissue changes, such as those met with in the various forms of interstitial nephritis, may be the result. As already stated, these forms merge one into another; in some cases the connective tissue changes predominate, although epithelial changes are always present; whilst in others the epithelial or glomerular changes are most marked; the interstitial changes, though attracting comparatively little attention, always accompanying them.

CLOUDY SWELLING OF THE PARENCHYMA OF THE KIDNEY

292. Cloudy swelling or "molecular," or "parenchymatous," degeneration of the kidney is one of the first results of altered nutrition and function of the renal epithelial cells, especially those lining the convoluted tubules. It may occur as an early stage of an inflammatory lesion, or it may be simply the precursor of fatty degeneration of the cells. The causes are much the same as those that induce cloudy swelling of the liver (§ 233) and of the heart (§ 256).

Naked-eye appearances.—The kidney is enlarged and rounded, the capsule strips off readily, leaving a peculiar shining opalescent pink surface. On section the cortex is seen to be enlarged and pale, though there is usually considerable hyperæmia, and the Malpighian bodies stand out prominently. The medullary rays are distinctly

seen, and the pyramids are deep in colour. The vessels in the boundary area appear to be filled with blood; otherwise the boundary and papillary layers are almost normal in appearance.

Harden (§ 62 or 63), (spirit alters the appearances of the cells, and should not be used as a hardening fluid for this tissue), and stain (§§ 102, 110 (*b*), and 132, and 164 or 165).

($\times 50$).—The principal changes are found in the cortex, where

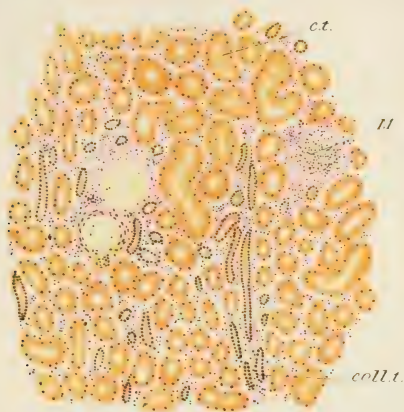


FIG. 108.—Cloudy swelling. Death during early stage of the process. Stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

c.t. Convoluted tubule in which epithelial cells are so swollen that the lumen is almost occluded. This swelling and the occlusion are well seen throughout. Cytoplasm cloudy and nuclei not so distinctly seen as usual.

coll.t. Collecting tubules, little altered.

M. Malpighian body slightly more prominent than usual, apparently because of numerous and more distinct nuclei.

the sections of the convoluted tubules present a greater surface than in the normal organ. The lumen is very irregular, and often appears to be little more than a star-shaped fissure. The epithelial cells are so swollen that the diameter of each cell is increased: its outline is irregular but very well defined.

($\times 300$).—The epithelial cells are greatly enlarged. They are angular, and so project into the tubule that the lumen may be almost obliterated. The outlining of the cells is distinct, the protoplasm

is much more granular than in the normal condition, and the nucleus is obscured, though in a few cases it takes on the nuclear stain very deeply, and may thus become more prominent. Treat a section with acetic acid (§ 189) or caustic potash (§ 190); the cloudiness disappears,

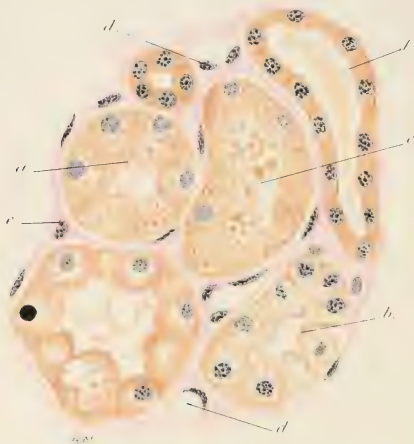


FIG. 109.—Cloudy swelling of the kidney, where death has taken place at a very early stage of the process. Stained with alum hæmatein and van Gieson's stain. ($\times 500$.)

- a.* Swollen columnar epithelial cells of a convoluted tubule. Outlines somewhat obscured; nuclei not very distinct; protoplasm coarsely granular.
- b.* Swollen epithelial cells, with apices projecting into the lumen of the tubule, giving rise to the radiate or stellate fissures very characteristic of this condition.
- c.* Coarsely granular protoplasm, breaking down.
- d.* Lumen of intertubular capillary blood vessel.
- e.* Basement membrane of capillary vessel and delicate connective tissue fibrils, hyaline, and much swollen.
- f.* Upper part of collecting tubule—intermediate—with hyaline cast lying in lumen.

and, with the exception of the change in size and shape, the epithelium regains its normal appearance.

If the change is of some standing—several days—a few clear highly refractile fatty globules stained black with osmic acid (§ 135), by which the nucleus is almost obscured, may be seen in the swollen

cell. From this it is evident that the cloudy swelling is being superseded by fatty degeneration, a condition met with in all cases of acute Bright's disease. The intertubular capillaries appear to be compressed, and around them a few leucocytes, which take on the carmine stain very deeply, may have escaped. In the medulla the vessels are more distended, and there is, frequently, slight catarrh, swelling, proliferation and budding off of young cells, but no other change in the epithelium of the straight tubules.

FATTY DEGENERATION OF THE KIDNEY

293. Fatty degeneration of the epithelium of the kidney is usually associated with imperfect nutrition, due to defective blood supply, or to the action of certain materials circulating in the blood; it often follows cloudy swelling, and, although it is sometimes said to be a simple condition, we must, from the nature of the change, and from the conditions with which it is associated, look upon it as being often closely associated with inflammatory processes. It is met with especially in patients who have succumbed to wasting diseases, such as cancer, phthisis, pernicious anæmia, Addison's disease, and diabetes; to certain fevers, such as scarlatina, typhoid and yellow fevers, and small-pox; or to the action of certain poisons, such as alcohol, sulphuric ether, phosphorus, arsenic, or antimony.

Naked-eye appearances.—These differ according to the stage of the degeneration. The kidney in the later stages is usually slightly smaller and paler than normal, and is extremely flabby. The capsule strips off readily. On section, the cortex may be normal in thickness, or slightly wasted, mottled, and somewhat yellow, and the surface flabby and greasy. On the yellow background the interlobular arteries with their double rows of Malpighian bodies stand out prominently; this gives a distinctly striated appearance to the cortical section, especially when the organ contains much blood (in phosphorus poisoning there may be small punctiform hæmorrhages in this position); in the medulla the striation is also well marked. Where this condition is associated with anæmia and wasting diseases, the pallor is more uniform than in those cases where inflammatory processes play a more prominent part.

Stain a section with osmic acid (§ 135), and then with carmine (§ 105), clear (§ 193) and mount (§ 199).

($\times 50$).—In the convoluted tubules the epithelial cells are

swollen, and contain droplets of fat (stained black with osmic acid)



FIG. 110.—Fatty degeneration of the kidney, from a case of diabetes. Stained with osmic acid and picro-carmin. ($\times 300$.)

- a.* Epithelial cells in the first part of a convoluted tubule, in which is well-marked fatty degeneration; smaller globules near the middle of the cell, larger globules near the basement membrane.
- b.* Cells in which there is infiltration, with large globules only, near the base of the cells.
- c.* Irregular, and *d.* straight tubules, in the cells of which there is no fatty degeneration.
- e.* Interlobular vessels, from which the afferent arteriole *f.* runs to supply the glomerular tuft *g.*, supported by a delicate connective tissue framework, and surrounded by an investing layer of epithelium, *h.*
- i.* Layer of flattened epithelial cells lining Bowman's capsule.
- k.* Thickened connective tissue and basement membrane of Bowman's capsule.
- l.* Slight increase of connective tissue at the point of entrance of the afferent arteriole.

of various sizes, principally at the bases of the cells, or near the basement membrane and blood vessels. Similar black dots are seen in the

Malpighian bodies, and in the epithelium lining Bowman's capsule. In the straight tubules the fatty change is not so well marked, and the globules are scattered throughout the substance of the cell: the collecting tubules usually appear to be unaffected.

($\times 300$).—The ring of dark globules at the periphery of the tubule

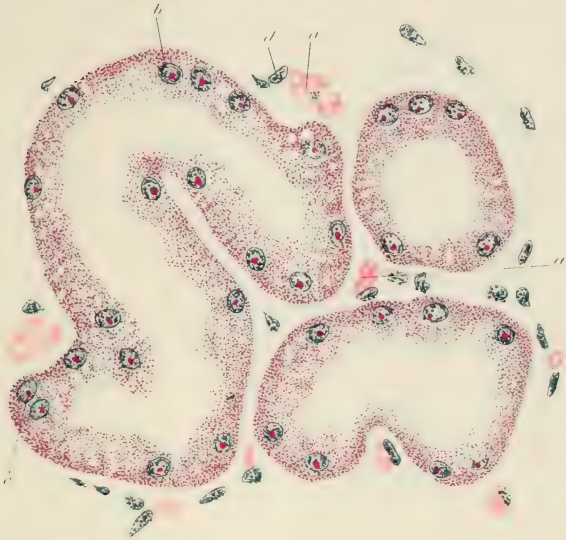


FIG. III.—Section of kidney, from a case of starvation (child). Fatty degeneration. Stained for granules by Muir's method (§ 165). ($\times 650$.)

- a. Intertubular capillaries, containing red blood corpuscles.
- b. Epithelium of convoluted tubule, containing fat, clear globules, and stained granules.
- c. Nucleus with red nucleolus of epithelial cell.
- d. Endothelial cell with large nucleus.

is seen more distinctly. It is composed of fat droplets of various sizes, some occupying a considerable portion of the cell, others being simply embedded in the cytoplasm: the nuclei in such cells are frequently obscured. The cells are very unequally affected, and a few may be comparatively healthy. Observe the granules in the epithelium lining

Bowman's capsule and in the walls of the capillaries. In the straight tubules the fat droplets are distributed irregularly throughout the protoplasm of the cell.

In metallic poisoning the fatty degeneration is much more marked, the whole of the protoplasm of the various cells may become fatty, not only in the tubule, but also in the capillaries and connective tissue; in such cases, small patches of blood corpuscles are met with as interstitial hæmorrhages, or as hæmorrhages into Bowman's capsule or into the tubules. In certain cases the degeneration is accompanied by fatty infiltration of the cells. As evidence of this, note the position of the fat globules, especially at the bases of the epithelial cells in the secreting or convoluted tubules. Treat sections with caustic potash (§ 190) and with acetic acid (§ 189). The fat is entirely unaffected.

Fatty degeneration, with atrophy of the epithelial structures of the kidney, is an extremely common condition; it has already been noted in waxy degeneration of the kidney; and it plays a very prominent part, not only in those inflammatory lesions which come under the heading of nephritis, but also in the numerous atrophic changes which are so commonly met with in this organ.

The lesions in Bright's disease are difficult to describe and equally difficult to follow unless the different types of inflammation can first be studied in their simpler phases. The most distinct types and the earliest changes are best seen in nephritis resulting from the action of certain poisonous substances, and amongst these the scarlatinal "poison" is one of the most important.

It will be well, therefore, to examine one or two forms of scarlatinal nephritis before giving a description of the more general forms.

ACUTE SCARLATINAL NEPHRITIS

294. The description of scarlatinal nephritis here given is based on the appearances presented in a kidney taken from a case fatal at the end of the first week after the onset of the fever, convulsions and death following suppression of urine. Such a case is the most acute type with which the pathologist has to deal.

Naked-eye appearances.—In some cases the kidney, except for a little hyperæmia, is perfectly normal in appearance. It has the same appearance as in cloudy swelling, but it is more congested; on section small hæmorrhagic patches are seen at the bases of the pyramids,

and scattered through the cortex. The Malpighian bodies are readily distinguished.

Harden (§ 61, 62, or 63) and stain two sections (§ 105), mount one (§ 195) and a second (§ 199).

($\times 50$).—The most marked changes are seen around the interlobular arteries. Examine these at their origin in the boundary layer



FIG. 112.—Acute scarlatinal nephritis; death on eighth day. Section stained with carmine, and mounted in Farrant's solution. ($\times 300$.)

- a.* Epithelium in an advanced state of cloudy swelling.
- b.* Commencing catarrh in the tubule, cells proliferating, some detached from the deeper cells, which are more or less flattened.
- a.i.* Interlobular artery, around which is a great amount of round cell infiltration.
- r.b.c.* Coloured blood corpuscles.
- t.c.* Section of atrophied tubule, compressed by the round-celled exudation.
- n.i.c.* Nuclei of intertubular capillaries, near which the round-cell infiltration is also well marked.

and as they pass towards the cortical surface. Around each are deeply-stained granular-looking areas, especially along the lines of the afferent arterioles. They also occur around the Malpighian bodies, and extend

from them for some distance between the surrounding convoluted tubules. Beneath the capsule and around the terminal branches of the interlobular arteries the granular areas are wedge-shaped, the base of the wedge being towards the cortical surface; in the boundary area are wedge-shaped granular patches, each with its base resting on the medulla, and its apex running upwards to meet the apex of the corresponding patch at the surface. The vessels in these patches are very prominent. Around the glomerular tuft, forming a kind of bounding line between the tuft and the enormous mass of granular material, Bowman's capsule is seen as a distinct, hyaline, translucent lamina, within which are numerous small pink dots (nuclei). At the point where the afferent arteriole enters the thickened Bowman's capsule there is frequently some thickening of the walls of the vessel. The tubules are filled with epithelium in a most typical condition of cloudy swelling (§ 292).

($\times 400$).—*Changes in the walls of the vessels.*—The interlobular arteries and the afferent arterioles stand out more prominently than in a normal kidney. Their transverse diameter is increased. This is especially well marked at the points where branches are given off, and near Bowman's capsule, and is due to—(1) hyaline swelling of the intima, which takes place irregularly along the course of the vessel; (2) infiltration of the muscular coat with leucocytes, lymphocytes, and connective tissue nuclei, and consequent thickening: this takes place especially near the entrance of the arteriole to the Malpighian body. Klein describes emboli in these narrowed vessels.

Changes around, and in connection with, the vessels.—The distribution of certain granular material was noted under the low power. The granules will now be seen to be polymorpho-nuclear leucocytes and lymphocytes, some of which have certainly escaped from the blood vessels; alongside them are found numerous coloured blood corpuscles; it is probable, however, that some of them have been brought up by the lymph channels, and that others are young connective tissue cells, derived by proliferation from pre-existing cells. This massing of the cells goes on not only around the glomeruli but also between the neighbouring tubules.

Changes in the Malpighian bodies or glomeruli.—The glomeruli are usually enlarged and deeply stained. The capillaries forming the tufts are swollen, whilst the intercapillary nuclei are increased in number. These are similar in all respects to those seen outside the

glomeruli, and are probably leucocytes which have migrated from the vessels as the result of the acute inflammatory process.

The basement membrane, or Bowman's capsule proper, is homogeneous and considerably thickened. At this stage cloudy swelling, and even proliferation of the flattened cells lining Bowman's capsule, is frequently met with.

The changes in the tubules are exactly those of cloudy swelling (§ 292) and slight catarrh (§ 291). In some of the tubules hyaline and blood casts are seen.

If the above conditions be looked upon as occurring in a less acute, and as gradually merging into a more chronic, form, the other conditions met with in scarlatinal kidney will be much more readily understood. The most important and initial changes are those which occur in and around the vessels and glomeruli, but they are always accompanied or followed by secondary changes in the epithelium. This and the advanced glomerular and connective tissue changes are well illustrated in the following.

SCARLET FEVER KIDNEY (No. 2)

295. Found in cases where death has taken place at from the seventh to the fourteenth week of the disease.

Naked-eye appearances.—The organ may be even smaller than normal, or only slightly enlarged. It is tough and dense, the capsule is readily removed, leaving the surface of the cortex pale or of a "pinkish colour, and more translucent than natural, on which the angular glomeruli may frequently be seen as brownish-red dots." (The glomeruli are never seen on the surface of the normal kidney.)

On section the superficial cortex may be normal in thickness, or it may be considerably narrowed, and is of much the same colour as the surface. The interpyramidal cortex, on the other hand, is usually swollen, in some cases markedly so, this often leading to compression of the bases of the medullary pyramids, which do not stand out so prominently as usual; it is of "opaque yellowish or pinkish-white colour, mottled with opaque yellowish-white points."

The enlarged glomeruli are usually distinctly seen in double rows on each side of the prominent interlobular artery. Some of them are translucent greyish, others brownish-red, angular dots. Where the

brownish-red dots are seen, patches of inflammatory exudation will be found surrounding the glomeruli. There are also angular yellowish patches, which represent to the naked eye the fatty and degenerative changes taking place in the epithelium of the convoluted tubules. The medulla presents a comparatively normal appearance, with the exception of the bases of the pyramids, where there may be some compression and irregularity.

Harden (§ 60 and 62 or 63), cut (§§ 57 (*a*), 82 *et seq.*), stain (§§ 102, 103 or 105 and 110 (*b*)), and mount (§ 195 or 199).

($\times 50$).—The principal changes take place in and around the Malpighian bodies, and along the course of the afferent arterioles and interlobular arteries, around which, and extending for some distance between the neighbouring tubules, as in the acute form, are seen the nuclei of polymorpho-nuclear and hyaline leucocytes and connective tissue cells, especially at the point of exit of the afferent arteriole. In some cases this increase of connective tissue nuclei and leucocytes may be enormous. Within the capsule they may also be increased in number, when, by pressure, they cause diminution in size of the vascular tuft. Some only of the Malpighian bodies are affected, and these very irregularly, according to the severity of the inflammation. The convoluted tubules immediately around the Malpighian bodies appear to be compressed by the products of inflammation around them, and exhibit marked catarrhal changes (§ 291).

Many of the convoluted tubules, and some of the straight tubules, are choked with broken-down or fatty catarrhal cells.

($\times 300$).—The swelling of the intima of the interlobular and afferent arterioles, described as occurring in the acute stage, may also be distinguished in this form. The nuclei of the inflammatory cells surrounding the vessels are, in many cases, in process of organisation into more or less highly developed connective tissue. Similar cells are present in great numbers around the Malpighian bodies, radiating from them between the interlobular vessels, or along the lines of the capillaries between the tubules. Bowman's capsule is swollen, hyaline, and homogeneous looking, in the later stages often becoming distinctly laminated. Within the capsule there seems to be an increase first in size, and then in number, of the flattened cells lining it, and within this again there is proliferation and partial organisation of the connective tissue cells supporting the capillaries, which become compressed and atrophied. The tubules near the Malpighian bodies are also atrophied

or compressed, and the epithelium is flattened; whilst there is, both in the straight and in some of the convoluted tubules, an accumulation of catarrhal cells, forming the so-called fatty and granular casts (§ 284 (2)). Along with the above conditions there is often simple catarrh in the straight collecting tubules. In this form the atrophy of the superficial cortex is said to be due to obstruction in the arterial system (§ 299).

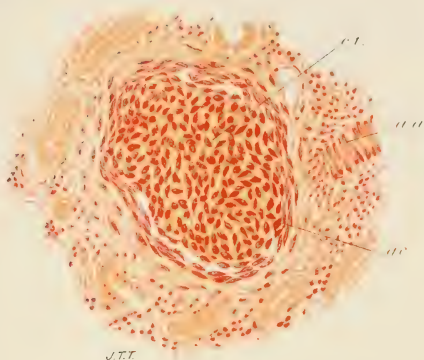


FIG. 113.—Post-scarlatinal nephritis; death at about the sixth week.
Stained with picro-carmin. ($\times 260$.)

- a.a.* Afferent arteriole, surrounded at its point of entrance to the glomerulus by a large number of leucocytes.
 - b.c.* Thickened Bowman's capsule, the endothelioid cells proliferating rapidly, and forming a distinct lining to the thickened and laminated capsule.
 - c.t.* Nuclei of connective tissue, supporting glomerular capillaries, greatly increased in number.
- Around the glomerulus are sections of tubules, surrounded by leucocytes, etc.

There is a form of acute interstitial nephritis met with at about the sixth week of an attack of scarlatina, in which the naked-eye appearances are very similar to those seen above, but the microscope reveals an extremely diffused form of acute interstitial and glomerular nephritis. The whole of the Malpighian bodies are affected, and between the convoluted tubules there is an extraordinary increase in the amount of young cellular connective tissue. In consequence of this the tubules are atrophied and widely separated, and the epithelium lining them is

in a state of active proliferation. Fatty casts may be seen in both the convoluted and straight tubules.

The more chronic forms of scarlatinal nephritis, occurring from six months to a year after the fever, are so like those met with in subacute interstitial nephritis, that it is unnecessary to give a separate description of them. The observer, however, should bear in mind that in the scarlatinal forms the glomerular changes, and the changes along the line of the interlobular vessels predominate, whilst in the other forms the interstitial changes are usually more "diffuse."

ACUTE PARENCHYMATOUS NEPHRITIS

296. Synonyms, "Acute Nephritis" or "Acute Bright's Disease," Acute "Desquamative," "Tubular," or "Catarrhal" Nephritis.

Of these names acute parenchymatous nephritis is undoubtedly the best, as it refers to the physical conditions found in the diseased organ, rather than to any theory as to the history of the disease.

It is found in patients who, during life, have high arterial tension, and pass albuminous and smoky urine, containing hyaline and blood or other casts. Causes,—sudden congestion, and overwork of the kidneys, irritant poisons, febrile conditions, pneumonia, and similar diseases. The earliest condition has already been described as cloudy swelling of the epithelium or "parenchyma" of the kidney (§ 292).

Naked-eye appearances in early but well-pronounced acute Bright's disease are—the kidney is "flabby" and considerably increased in size, especially in thickness,—it is more rounded; the capsule is tense, but strips off, even more readily than usual; the surface is pale and œdematous, and has a peculiar mottled appearance, and on this pale background the *venæ stellatæ* stand out prominently; cysts are seldom met with. On section the cortex presents a peculiar granular mottling; it is both relatively and absolutely much increased in thickness, and, although large quantities of blood escape from the cut vessels, it is pale when the blood is washed away; on the pale pink background are "opaque pinkish points" and "markedly injected dots, due to the swollen vessels and glomeruli." If the process is very acute, small hæmorrhages are found in the cortex, the whole of which may be intensely injected and red. The medullary portion of the kidney is simply congested, and is rarely affected by any graver changes at this

stage. The mucous membrane of the pelvis of the kidney, however, is much injected.

Harden (§ 62 or 63), stain (§§ 102, 104, and 135), and mount (§ 195 or 199).

($\times 50$).—In the cortex, and that part of the boundary layer in which the epithelium of the (convoluted) tubules is columnar, the following changes may be noted. There is cloudy swelling (§ 292) of some of the cells; others are undergoing rapid proliferation, and the large swollen cells are dividing (the early stage of catarrh) (Fig. 109). In these dividing cells there is evidence of degenerative change—the swollen cytoplasm is granular; in many cases this is so marked that the epithelium is opaque and the nuclei are obscured. In the opaque masses of cytoplasm small oil droplets are frequently seen, especially if stained with osmic acid. Blocking up some of the tubules are masses of broken-down fatty cells, which accumulate to form a kind of plug. The interlobular vessels and afferent arterioles are distended; the Malpighian bodies also appear to be considerably larger from the increased quantity of blood which is contained in their capillaries. Around the glomerular capsules, and between the convoluted tubules, especially near the surface of the cortex, small pink dots (polymorphonuclear leucocytes, lymphocytes, and nuclei of young connective tissue cells) are more numerous than usual, pointing to the fact that along with the parenchymatous inflammation there is, even at this early stage, some interstitial change. In some of the Malpighian bodies, and in or around some of the convoluted tubules, are masses of blood corpuscles, which have passed out from ruptured blood vessels. In some cases a mass of brown pigment is all that is left to represent this blood, especially in the straight tubules. Tube casts (hyaline fibrinous, blood, and a few fatty, casts (§ 284)) are met with in the convoluted tubules, and also in smaller numbers in the straight tubules, whither they have been washed down by the urine. The vessels in the medulla are filled with blood.

($\times 300$).—All the above conditions are more readily recognised. The congestion of the vessels in both cortex and medulla, the crimson nuclei around the Malpighian bodies, the slight separation of the convoluted tubules, the swollen, extremely granular or proliferating and slightly fatty cells in the convoluted tubules and ascending tubule of Henle, the casts of various forms—hyaline, seen as very transparent material, fatty, in which the outlines of the cells may still be made out—and the blood casts or masses of altered blood, in the convoluted

and straight tubules (§ 284 (1)), and the slight increase in the amount of

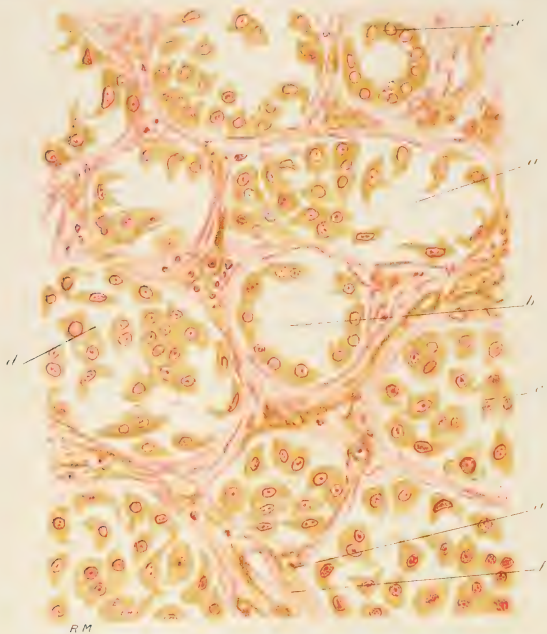


FIG. 114.—“Catarrhal” nephritis in which interstitial changes may also be observed. Stained with picro-carmin. ($\times 300$.)

- a.* Oblique and *b.* transverse section of a convoluted tubule in which there is well-marked catarrh.
- c.* The proliferating cells have assumed a cubical character, the layer which remains attached to the basement membrane being that from which new cells are developed.
- d.* The cells are more irregular in shape, but even here is a flattened or spindle-shaped layer from which, under certain conditions, new secreting cubical or columnar cells might be developed. Even in the most advanced stages we find some trace, however imperfect, of an epithelial lining left.
- e.* Section of straight tubule, in which there is little catarrh.
- f.* Swollen fibrous tissue; in addition to swelling, however, there is an actual increase of fibres formed by proliferating connective tissue cells (*g*).
- g.* Leucocytes and connective tissue nuclei.

interstitial connective or fibrous tissue.

SUBACUTE (OR CHRONIC) PARENCHYMATOUS NEPHRITIS

297. Synonyms, "Large Pale" (?) Kidney or "Fatty" Kidney.

The acute form of Bright's disease may be cured; sometimes, however, it is followed by a series of more chronic changes, when we have what is spoken of as the "large pale" or "fatty" kidney. These are both faulty names, as the waxy kidney, and the kidney of subacute interstitial nephritis, which is even paler than that of chronic parenchymatous nephritis, are both spoken of as large pale kidneys, whilst the fatty change in the epithelium is common to this and to many other forms of diseased kidney. Of the two names, however, the latter is preferable. Although this form of Bright's disease may follow the acute form, it is far more frequently met with as a subacute condition from the outset, when it runs a very definite and usually fatal course.

Naked-eye appearances.—The kidney is considerably enlarged. The capsule is still readily separable. The surface is pale, mottled, and somewhat anæmic. On section, the cortex is swollen, and is mottled pink and yellow. The Malpighian bodies are not more prominent than usual. On taking scrapings from the cut surface and floating them in water, greasy streaks are seen. There is now no congestion of the pelvis of the kidney.

Harden (§ 62 or 63), cut (§§ 57 (*a*), 82 *et seq.*), stain (§§ 102, 104 and 135), and mount (§ 195 or 199).

($\times 50$).—In the section stained with osmic acid, fatty globules may be seen in the degenerated epithelium of the convoluted tubules of the cortex. The vascularity between the tubules is not great, but the nuclei around the Malpighian bodies, and around the tubules, are increased in number, and there is an increase in the amount of connective tissue. Some of the tubules are comparatively open, and are lined by a layer of flattened cells, which take on the nuclear stain very readily, even those which are choked with the blackened epithelium are seen to have this layer of flattened cells lining the tubule. The casts in the tubules are more colloid and fatty than in the earlier stages of the disease. They are especially numerous in the lower part of the convoluted tubules, and in the first part of the straight tubules.

($\times 300$).—The epithelium lining the convoluted tubules is flattened, and forms a thin cellular layer around the lumen, or around the mass of fatty material occupying it. These flattened cells are young epithelial cells, and, as a rule, are not granular or fatty. This layer is seldom or

never thrown off, *i.e.* complete degeneration does not take place, the cells remain, and from them any new epithelium that is formed is reproduced. The colloid and other casts (§ 284 (2)) are stained yellow. Verify the other conditions seen under the low power, more especially the cellular increase around the Malpighian bodies and around the tubules. Look for dilated tubules above points blocked by the tube casts.

In the straight tubules the cells may also present this flattened appearance, and casts of small cells are frequently met with.

SUBACUTE INTERSTITIAL NEPHRITIS

298. Synonym, "Large, Pale, Smooth" Kidney following acute Bright's disease. From the description given of the second stage of parenchymatous nephritis, the student will be quite prepared to meet, at a still later period of the disease, with considerable increase in the amount of connective tissue (formed from the proliferating cells around the blood vessels), especially between the convoluted tubules.

Naked-eye appearances.—The organ is usually slightly enlarged, and is firmer than normal. The capsule may be somewhat thickened and adherent; the surface is pale with yellow mottlings, but the venæ stellatæ are congested. On section the cortex is seldom thickened, and is usually atrophied, the Malpighian bodies are not prominent, and the tissue of the cortex is firm, dense, and translucent. Small cortical cysts are sometimes met with, but not nearly so frequently as in the granular contracted kidney (§ 299).

The arteries of the boundary layer have rigid and thickened walls, and always remain patent and prominent, and there is some congestion at the bases of the pyramids.

Harden (§ 62 or 63) and stain (§§ 102 or 103 and 108 *et seq.*).

($\times 50$.)—The Malpighian bodies have the normal arrangement, but they are undergoing very important changes. These changes will be more readily understood if a general description of the appearances of the cortex be first given.

In the deeper part of the cortex, along the lines of the interlobular arteries, are wedge-shaped masses of solid-looking tissues, with the base directed towards the medulla. Dipping down from the surface is a similar wedge, the base of which is at the cortical surface, the apex running down to meet the apex of the other pyramidal mass.

Between these more solid-looking areas are oval patches of comparatively normal and open tissue, which are situated midway between



FIG. 115.—Section of a kidney from a case of subacute interstitial nephritis, showing well-marked glomerular change. Stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

i.d.. Interlobular artery, longitudinal section.

On each side of this artery is fibro-cellular connective tissue (*c.c.t.*), ultimately contracting or cicatricial tissue. In this new tissue are numerous atrophied tubules (*a.t.*) of various types. In some of the convoluted tubules colloid casts (*c.c.*) may be seen.

M. Glomerular tuft, with increased number of nuclei.

B.C. Bowman's capsule greatly thickened through proliferation of the lining endothelial cells.

M'. Glomerular tuft with closed capillaries, the whole mass having become fibroid.

the interlobular arteries, and consequently are composed of sections of straight tubules in the centre, and of convoluted tubules at the

margin. The convoluted tubules, especially those near the margin of the denser tissues are considerably dilated. In the denser areas the small openings are lined with flattened fatty and atrophied cells; these are sections of compressed and atrophied convoluted tubules. Arranged fairly regularly along each side of the interlobular arteries are the Malpighian bodies, in some of which very marked changes have taken place; others appear to be healthy. The healthy tubes are almost invariably situated in the open, more normal tissue. Those which are situated between the open and denser tissue, or just within the margin of a denser area, are often somewhat increased in size, owing to an increase in the connective tissue of the glomerular tuft, and to distension of the capsule by an accumulation of colloid matter or fluid. In the middle of the denser wedge-shaped area the Malpighian bodies are usually much diminished in size, and are packed more closely together than usual. Bowman's capsule is seen to be very much thickened and fibroid, and in many cases the glomerular tuft cannot be discerned at all, or only as a small knot of fibrous tissue. Between the atrophied tubules and the altered Malpighian bodies there is an enormous amount of small round-celled or young connective tissue which appears to be in process of organisation; this does not seem to affect the Malpighian bodies specially, but is distributed along the lines of the interlobular and intertubular vessels. It is this tissue which gives the solidity to the wedge-shaped masses. In the boundary layer the larger branches of the blood vessels have thickened walls; there appears to be thickening in all three coats, in consequence of which the lumen is somewhat narrowed.

($\times 300$).—Within Bowman's capsule note the layers of new fibrous or hyaline tissue, and, within these again, numerous cells. At some points the fibrous tissue may be absent, and there is simply a thicker, often irregular, layer of cells lining the capsule. The thickening may be due—(1) to a growth by multiplication of the layers of flattened cells within the capsule; (2) to proliferation of the connective tissue cells around Bowman's capsule, which thus brings about a thickening of the "adventitia" of the Malpighian body; (3) to a deposition of inflammatory coagulable lymph in layers between the glomerular tuft and Bowman's capsule; the leucocytes or detached epithelial cells stand out quite distinctly from the granular or hyaline fibrin in all stained specimens; this is not very frequently

met with, but it undoubtedly occurs in certain very acute cases; or (4) to the thickening of the basement membrane of the capsule. The periglomerular infiltration is well marked, as is also the rapid proliferation of the connective tissue cells, which support and invest the glomerular capillaries. This latter may be so marked, indeed, and

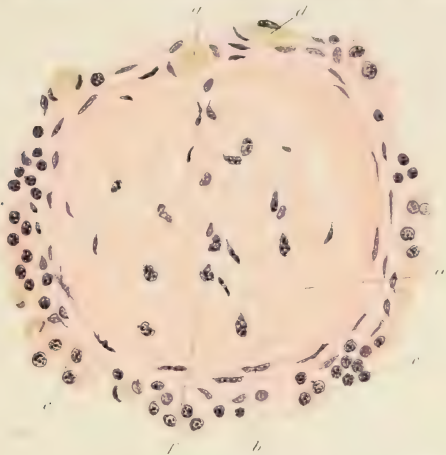


FIG. 116. — "Fibroid" Malpighian body from a case of subacute interstitial nephritis. Stained with alum hæmatein and van Gieson's stain. ($\times 250$.)

- a.* Thickened hyaline or fibroid laminated capillaries of glomerular tuft—occluded.
- b.* Nucleus of endothelial cell of Bowman's capsule, lying on swollen and laminated basement membrane, and helping to bring about thickening of the capsule.
- c.* Section of atrophied convoluted tubule.
- d.* Interlobular capillary blood vessel.
- e.* Small mononuclear cells lying between tubules and basement membrane of Bowman's capsule.
- f.* Nuclei of cells covering or lying between occluded glomerular capillaries.
- g.* Transverse section of afferent arteriole.

its organisation so far advanced, that the capillaries are atrophied by pressure, and nothing but a firm fibrous knot, around which the capsule may be firmly contracted, remains; this knot may be situated at one side of the capsule, which is then distended to form a small cyst filled with colloid or watery material.

Changes in and around the tubules.—The basement membrane may be swollen and hyaline looking; the epithelium, though proliferating rapidly in the earlier stages, and forming irregular cells, does not

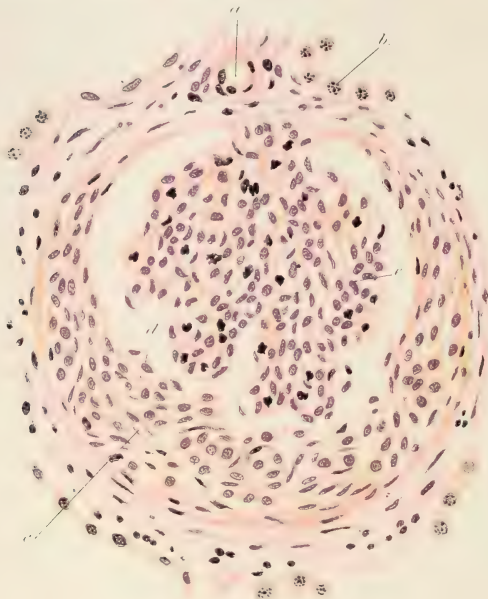


FIG. 117.—Glomerulo nephritis. Proliferation of the cells of Bowman's capsule. Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Afferent arteriole, slightly thickened.
- b.* Epithelial cells lining convoluted tubule.
- c.* Thickened Bowman's capsule.
- d.* Proliferating cells lining Bowman's capsule.
- e.* Contracted glomerular tuft with proliferating lining and investing cells.

desquamate, for in carefully hardened sections a distinct epithelial layer is always seen; the cells of this layer may be somewhat irregular in shape and size, but in the later stages they become much flattened.

Numerous fatty and colloid casts are found in the various parts of the convoluted and straight tubules.

Changes in the connective tissue.—Along the lines of the capillaries, and between them and the basement membrane of the tubules, embedded in the small round cell tissue, are numerous branching cells or more fully developed connective tissue cells, of which there are so many in an undeveloped condition around the Malpighian bodies and the atrophied tubules; they may form a firm fibrillated connective tissue. Secondary to this fibrous tissue formation, the capillaries become atrophied, though some of the intertubular vessels still remain patent. It must be remembered, however, that these connective tissue changes are often secondary to changes in the blood vessels.

Changes in the arteries and arterioles.—The inner coat within the internal elastic lamina is often thickened. (See Endarteritis Obliterans, § 273.)

Frequently there is pseudo-hypertrophy of the muscular coat, due to an increase in the number of connective tissue cells between the muscle fibres, which may be much atrophied.

As already noticed, there is a general increase in the interstitial connective tissue; and the tunica adventitia of the arteries, which is really a part of, or is directly continuous with, this interstitial tissue, takes part in the general thickening.

It is held by some authorities, with a considerable show of reason, that this form of interstitial nephritis is but an early stage of the granular contracted kidney. As this seems to be especially the case as regards the large granular kidney, it will not be necessary to say anything of that form beyond referring to the diminution in size of the organ, especially of the superficial cortex, the granular surface, the thickening, lamination, and adhesion of the capsule, the more advanced glomerular, vascular, and interstitial changes, and the more numerous casts.

GRANULAR CONTRACTED KIDNEY

299. Chronic Interstitial Nephritis? "Cirrhosis" of the Kidney? "Small Red" Kidney, or "Gouty" Kidney is found especially in alcoholics, in gouty patients, and in cases of chronic lead poisoning.

Naked-eye appearances of the small or typical form.—The kidney

is very much diminished in size, and its substance is extremely tough. The capsule is thickened, opaque, and laminated, and is firmly adherent to the subjacent tissue, so that it comes away in layers, shreds remaining adherent to the cortex, or else bringing away with it fragments of the parenchyma, leaving a very granular surface, which feels like a piece of moist morocco or shagreen. The granules are pale, small, and fairly regular in size, each corresponding to a lobule; the fossæ around them are usually injected, and much redder in colour than the elevated patches or granules. It is to these red patches that the capsule is most firmly adherent, and at these points small vessels appear to run from the capsule into the tissue beneath. Over the surface of the kidney there may be deeper and more irregular sulci, which divide it into areas, these usually corresponding accurately to the outlines of the lobes of which it is made up. On the surface numerous cysts are seen; the sizes of these vary from a pin point to a walnut, or even larger; small brick-red or yellow points (uratic deposits) are also seen scattered over the surface.

On section, the cortex, which is tough and leathery, is much contracted; it may be only a sixth of the normal thickness; the thinning of the cortex is most marked at the bases of the pyramids. The edge of the cut surface is sharply defined, but uneven, the elevations corresponding to the granules already described. The section varies very greatly in colour, but in a very large proportion of cases it is brick-red, and is not specially anæmic. Small cysts, most of them filled with a yellow gelatinous material, and brick-red or yellow lines (deposits of urates in the tubules), are scattered at irregular intervals over the cortical surface; similar yellow lines, but straight, are also seen in the medulla. Notice further that the parallel radiating lines, composed of the straight tubules and double rows of Malpighian bodies, are either altogether obliterated, or are tortuous and irregular, and that the interlobular arteries are thickened and much distorted. This irregularity is characteristic of the disease, and even in the early stages, when no other naked-eye evidence can be made out, it is quite sufficient to indicate the presence of atrophy. The large branches of the renal artery are rigid and atheromatous; those in the boundary layer have their walls thickened, and the lumen patent, so that they stand out much more prominently than would vessels in the normal kidney. The interpyramidal cortex is pale, often swollen, and atrophied only in the very late stages of the disease.

The medullary pyramids are usually somewhat atrophied, especially near their bases, but present no marked naked-eye changes. In the



FIG. 118.—Section of granular contracted kidney. Stained with alum hæmatein and picro-erythrosin. ($\times 20$.)

This section includes one of the solid wedge-shaped areas passing in from the surface along the line of the interlobular artery.

- a.* Thickened and laminated capsule.
- m.a.* Atrophied Malpighian body, with cellular tissue and atrophied tubule around.
- m.b.* Normal Malpighian body outside wedge-shaped solid area.
- m.c.* Cystic space around atrophied Malpighian body at margin of wedge-shaped area.
- c.t.* Open or even dilated convoluted and collecting tubules, some containing casts.
- o.a.* Section of thick walled artery, with endarteritis obliterans and thickening of the adventitia.

pelvis there is frequently more fat than is usually present around the calyces.

Harden (§ 62 or 63), stain (§§ 103 and 106), clear (§ 193), and mount (§ 199).

($\times 20$).—The free cortical surface is very irregular, with elevations and depressions corresponding to the granules already mentioned; the capsule is thickened, firmly adherent to the wedge-shaped patches beneath, laminated and stained with nuclear stains. Running from the depressions down along the lines of the interlobular arteries are wedged-shaped patches of dense granular-looking tissue, the base of the wedge being situated towards the cortical surface. Between these dense areas are patches more or less oval, which are evidently com-

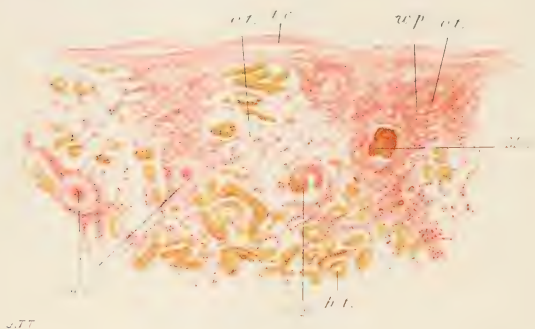


FIG. 119.—Part of cortex of granular contracted kidney. Stained with picro-carmine. ($\times 40$.)

- t.c.* Thickened capsule, laminated and adherent, especially over the dense wedge-shaped areas.
- w.p.* Wedge-shaped patch, composed of atrophied tubules (*a.b.*) and fibroid Malpighian bodies (*M.B.*)
- o.t.* Ovoid patch of open tissue, composed of dilated convoluted tubules, from which most of the epithelium has fallen out.
- C.B.* Enlarged Malpighian body, early cyst formation, situated at the margin of the more solid patch.
- h.t.* Comparatively healthy tubules.

posed, as in the case of subacute interstitial nephritis, of sections of the straight and some of the convoluted tubules, either normal in size or greatly distended. It will be sufficient for our purpose to describe one of these dense patches and one of the open networks along with the vessels in the boundary layer. Begin at the centre of the patch, and work outwards; it will be noted that the centre is occupied by the interlobular artery, which is somewhat thickened and tortuous. Around this the Malpighian bodies appear to be massed

closely and much more irregularly than normal. The Malpighian



FIG. 120.—Section of kidney. Chronic interstitial nephritis.
Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- a.* Thickened and laminated fibrous capsule.
- a.t.* Atrophied tubules containing colloid casts.
- M.* "Fibroid" Malpighian body.
- c.a.* Artery with thickened walls, endarteritis obliterans.
- c.c.* Dilated convoluted tubule containing colloid cast.
- f.c.t.* Fibro-cellular tissue in which are numerous atrophied, and some dilated, tubules.
- c.t.* Dilated collecting tubules containing hyaline casts.

bodies nearer the surface of the kidney and nearer the interlobular

vessel are represented by a diffusely stained point only, whilst those situated nearer the margin of the dense mass are surrounded by



FIG. 121.—Section of granular contracted kidney, showing part of the wedge-shaped fibro-cellular area along the line of an interlobular artery. Stained with alum hæmatein and picro-erythrosin. ($\times 150$.)

- a.* Interlobular artery.
- f.c.t.* New fibro-cellular tissue in which are numerous atrophied tubules.
- v.* Interlobular vein.
- a.t.* Small branch of artery with thickened wall.
- M.* "Fibroid" Malpighian body around which Bowman's capsule is somewhat thickened.
- c.t., c.t.* Convoluted and collecting tubules greatly dilated. These are all situated at the margin of the solid area.

thickened capsules, and may be smaller than normal, or their atrophied tufts of vessels may be contained each within a large cyst formed of the distended and thickened Bowman's capsule. In the

centre of the small rounded areas of granular material, which are not so opaque as the surrounding tissue, are some very minute openings. These are the atrophied convoluted tubules, which are lined with flattened epithelial cells. The tubules in the open network between the denser patches are, in some instances, enormously distended, and are also lined with flattened epithelial cells. The irregularity and tortuosity of the medullary rays, as they pass to the surface, are in great measure due to the unequal dilatation of some of these tubules, combined with the contractions which take place in the fibroid or denser patch.

($\times 300$).—The thickened capsule has a peculiar hyaline appearance. The dense patch is composed principally of atrophied tubules and Malpighian bodies. Between these, however, there is a slight increase of small round cells which, in certain forms, appears to follow the atrophy of the tubules; but in others the process is similar to the subacute interstitial change, though of a more chronic nature. It is frequently exceedingly cellular or almost granular in appearance, even under the high power, and very little fully formed fibrous tissue is observable. In this denser patch the intertubular capillaries may be obliterated at points, but, to make up for this, there is an accession of small branches from the capsule; these run into the patch at the most retracted parts, and appear to communicate with the terminal branches of the interlobular arteries. The Malpighian bodies, as already seen, present three distinct forms—(1) the pink ring composed of fibrous concentric laminae, in the centre of which is the yellow atrophied knot of capillaries; (2) the enormously thickened and fibrous capsule, with the capillary vessels of the tuft still patent; and (3) the thickened and distended capsule, with the capillary tuft lying within, but only partly filling it. The method of formation of the thickened capsule has already been referred to (§ 298). The tubules found in the dense mass are in various stages of atrophy. The lumen is small, the epithelium is flattened or irregular, and is undergoing fatty degeneration, whilst numerous colloid casts are seen in the tubules. The basement membrane is swollen and hyaline. Casts of a similar nature are found in some of the dilated tubules which form the open network, and are lined by flattened, often fatty, epithelium. On careful examination, the larger arteries will be found in a condition similar to that met with in subacute interstitial nephritis (§ 298). The intima is thickened—endarteritis obliterans (§ 273); there is an apparent hypertrophy of the middle coat consisting in an increase of the connective tissue cells and a hyaline

swelling of the connective tissue fibrils between the muscle fibres, which are often somewhat atrophied; the adventitia, which is continuous with the surrounding connective tissue and Bowman's capsule, is also hyaline and increased in thickness.

Notice that here we have an exceedingly chronic process, which appears to consist primarily of an atrophy, first of the Malpighian bodies and then of the tubules, followed, very gradually, by a slight increase in the amount of connective tissue. The changes in the Malpighian bodies are, in turn, due to the changes in the terminal branches of the interlobular arteries, around which, near the surface, the first indications of the disease are seen; the process gradually spreads down to the medulla, which thus, at a later stage, may become involved. This *atrophic* form of *granular contracted kidney* appears to be quite distinct from the so-called *large granular kidney*, in which the process is preceded or accompanied by a considerable increase in the amount of connective tissue, and which is more like the subacute interstitial nephritis, of which it is more than possible that it is the chronic continuation, more or less acute exacerbations occurring at intervals. In such a case, the interstitial changes are more diffuse than in the true granular or atrophic form; there is not the same tendency to contraction, though the newly formed connective tissue undoubtedly does contract, and so may give rise to secondary atrophic changes. It is, in fact, essentially a chronic interstitial nephritis.

TUBERCLE OF THE KIDNEY

300. Tubercle occurs in the kidney as one of two forms—(1) disseminated or acute miliary tuberculosis; or (2) tuberculous pyelo-nephritis.

(1) The disseminated form occurs most frequently as part of a general tuberculosis; in which case the affection of the kidney is, as a rule, late, and of comparatively little importance.

Naked-eye appearances.—The organ is not enlarged or markedly altered in any way. On stripping off the capsule, small grey granulations, about the size of a millet seed, are seen projecting, very slightly, above the surface. On section these grey granulations are wedge-shaped, and extend down into the cortex for some distance along the lines of the interlobular arteries. Similar masses may be situated more deeply in the cortex, where they assume an elongated or oval form; deeper still in the boundary layer they are rounded; they are seldom

found in the medulla. In some cases they are surrounded by a distinct hæmorrhagic zone, especially in the later stages, when they become opaque, and white or yellow in the centre. Nodules (fibromas) similar in appearance but more translucent, are frequently found in the centre of the pyramids; but these are much firmer, and, on microscopic examination, are found to be composed of fibrous tissue.

Harden (§ 58, 62, or 63), stain (§ 102, 103, or 104), and mount (§§ 195 or 193 and 199).

($\times 20$ and $\times 50$).—It is at once seen that the tuberculous process is going on around, and in connection with the distribution of, the

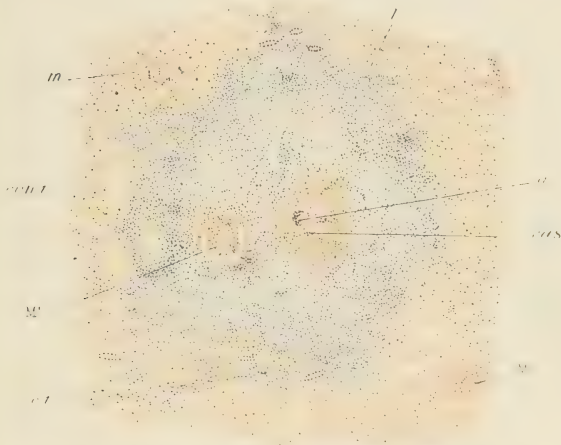


FIG. 122. —Tubercle of the kidney. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- g.* Giant cell in centre of tubercle follicle.
- cas.* Tissue undergoing caseous degeneration.
- M.* Malpighian body surrounded by tuberculous tissue.
- l.* Leucocytes and lymphocytes at margin of tubercle follicle.
- M.m.* Malpighian bodies, normal.
- con.t.* Convoluted tubules, normal.
- c.t.* Collecting tubules, normal.

interlobular arteries. Each of the small opaque-looking nodules, around which are evidences of interstitial inflammation, is made up of several tubercle follicles. The tuberculous giant cell structure can sometimes be made out, but in this organ caseation takes place at a

very early stage of the process. The cells—of which the young non-caseated tubercle follicles (when present) are composed—may be seen to differ very considerably in both size and structure. Near the centre are numerous so-called endothelioid cells of irregular shape, each containing several nuclei, and frequently lying on delicate filaments of pink tissue. Around are numerous smaller cells; between these the pink fibrillar tissue is distinctly marked, especially at the outer part of the follicle, where it forms a kind of capsule. Small homogeneous or granular yellow caseous patches may often be seen in the centre of the follicle, even in the very early stage of the growth, when nothing can be made out but a mass of small rounded cells, with here and there a few of the larger endothelioid cells near the centre. In some few cases the typical giant cell formation (see Liver, § 246) may be developed before caseation sets in; but in the kidney this is comparatively rarely met with. The softened points gradually increase in size, until several of them run together, and small cavities are formed; this is not of very frequent occurrence. Notice especially the arrangement of the tuberculous nodules along the lines, and in the perivascular sheaths, of the interlobular arteries.

($\times 300$).—Examine the constituent elements of the tubercle follicle more carefully, noting the endothelioid cells of various shapes and sizes with several nuclei; between and supporting these cells is delicate fibrillar tissue; at the periphery of the mass the small round cells with denser fibrous tissue between them are well seen. If there is a true giant cell system, the structure is similar to that met with in the liver (§ 246). Note carefully that these tubercle masses have no vascular supply, the arteries having become obstructed, and that the caseation takes place in the centre of the nodule, or in those follicles which are farthest removed from the blood vessels at the periphery of the nodule.

(2) Tuberculous Pyelo-Nephritis—synonyms, “Genito-Urinary Phthisis,” “Genito-Urinary Tuberculosis,” “Scrofulous” or “Strumous Pyelitis,” “Renal Phthisis” (not a good term), “Chronic Localised Tuberculosis,” etc.—is usually associated with tuberculosis of the ureter, of the trigone of the bladder, and of the vasa deferentia and vesiculæ seminales (scrofulous testicle). Both kidneys may be affected, usually, however, unequally.

In the earlier stages of the disease small yellow caseous nodules, with minute cavities in the centre, are situated towards the bases of the pyramids; these extend upwards and downwards in the calyces and in

the pelvis along the lines of the lymphatics in the submucous tissue. Ulceration soon follows this caseation; similar grey nodules, which soon begin to caseate, are also found in the pelvis of the kidney, the surrounding injection of the mucous membrane often being a very marked feature.

Harden a piece of the wall of a cavity (§ 58, 62, or 63), stain (§ 103 or 104), and mount (§ 199).

($\times 50$).—The caseous centres are stained yellow, and are composed of a mass of granular débris. Beneath this are seen tubercle follicles which appear to undergo caseation at a very early period of development. Giant cells are rarely met with in the kidney, but if a piece of tuberculous testicle from the same case be examined, giant cell systems are seen to be exceedingly numerous. The origin of the disease is as yet imperfectly understood; but it appears that there is a local tuberculous process beginning in the mucous membrane (the result of impaction of tubercle bacilli in one of the small blood vessels), followed by early caseation and rapid ulceration; after which the process may spread by the blood vessels, by the lymphatics, or by direct contact. It is possible, however, that catarrh may be the starting-point of the disease, this being followed by a tuberculous infection.

In the fully developed disease the kidney is very much enlarged and lobed, a marked depression existing between the projections, which vary in diameter from three-quarters of an inch to one and a quarter inches. The capsule may strip off readily, leaving a pale smooth surface, from which the *venae stellatae* stand out prominently, or it may be slightly adherent. On section each nodule is found to correspond to a caseous mass or to a rounded or irregular cavity, and each depression to a kind of septum, which corresponds in position to the interpyramidal cortex, the cavities occupying the position of the Malpighian pyramids. Each cavity contains a yellowish or purulent-looking fluid in which float caseous fragments; its walls are rough and finely nodulated or papillated, or are ragged looking; they are lined by a soft, dirty yellow or caseous material, which may be readily removed with the finger-nail as a soft putty-like mass. The pelvis of the kidney is lined by a similar material, and is usually considerably distended. The ureter, too, has its walls thickened, is blocked with the same caseous material, and feels like a hard firm cord. The microscopic appearances are those presented by rapidly growing and caseating tubercle.

SUPPURATIVE NEPHRITIS

301. Surgical kidney, a condition of suppurative nephritis, occurs very frequently in connection with stricture of the urethra, or renal or vesicular calculus; these causing pyelitis (inflammation of the pelvis of the kidney), or cystitis (inflammation of the bladder), in which the contents of the bladder undergo putrefactive changes as the result of the entrance of bacteria from without. The septic inflammatory process is supposed to pass back along the ureter to the pelvis of the kidney, and thence by the collecting tubules to the secreting tubules. It is probable, however, that the lymphatics and blood vessels are really the channels by which the bacteria are carried to the parenchyma of the kidney from the mucous membrane of the pelvis. This condition is also known under the following names:—"Disseminated Suppuration" of the Kidney, "Multiple Abscesses" of the Kidney, "Suppurative Pyelo-Nephritis."

The kidney is usually, though not always, irregularly swollen; it is soft, sodden, and friable, and the capsule strips off readily. The vascularity varies very considerably at different parts. On the surface small projecting yellow points may be seen surrounded by deeply injected or hyperæmic zones. On pricking one of these yellow points a small drop of pus escapes.

On section most of the yellow points are found in the cortex, where they assume a wedge shape, but a few elongated abscesses are also seen in the pyramids. Around each abscess the hyperæmic zone is well marked; where the condition is more advanced, the kidney may have the above characteristics exaggerated, whilst the small cavities have run together, and may replace a considerable part of the kidney tissue. Where the abscesses are of considerable size, they usually communicate with the pelvis of the organ, and contain ammoniacal phosphates mixed with the pus (pyo-nephrosis), or they may extend into the surrounding tissue, giving rise to the so-called peri-nephritic abscesses, which, however, most frequently occur quite independently of this condition. The mucous membrane of the pelvis is usually widely infected, even before the abscesses are well formed in the kidney itself, and small grey swollen points or yellow specks of pus may then be seen in the submucous connective tissue.

Harden (§ 58 or 63), stain (§§ 102 or 103, and 173 or 118), and mount (§§ 195 or 193 and 199).

($\times 50$).—In the cortex much granular material (deeply stained



FIG. 123.—Section of the cortex of a kidney in which are septic emboli from a case of acute miliary suppurative nephritis, the result of ulcerative endocarditis. Stained by Gram's method and with alum haematein and van Gieson's stain as contrast stain. ($\times 20$.)

- a.* Mass of micrococci impacted in small blood vessel. Around this we have marked accumulation of leucocytes. There is great congestion of the vessels near this commencing abscess.
- a.v.* Section of one of the vascular arches in the boundary area.
- Masses of micrococci in the straight vessels in the boundary layer. The epithelial lining of the tubules, except in the immediate neighbourhood of the commencing abscesses, is comparatively healthy, or is simply undergoing cloudy swelling.
- a.p.* Small abscess with dead cells, etc., in its centre.
- c.* Capsule, swollen and hyaline.
- cont.* Convoluted tubule.
- c.t.* Collecting tubules.
- Distended capillaries of glomerular tuft crammed with micrococci.
- M.* Malpighian body with slight increase in number of nuclei.
- M'.* Malpighian body in which capillaries are blocked by septic emboli.

with nuclear stains) may be seen running along each side of the interlobular arteries surrounding the Malpighian bodies, and also in between the convoluted tubules, which thus become widely separated from one another. This is most marked at the bases of the pyramids. Within the tubules the epithelium is granular, and appears to be undergoing a process of disintegration. Similar changes are seen in the medullary portion of the kidney along the lines of the vasa recta, thence extending between the straight tubules. In some cases the changes are so grave that a mass of deeply stained granular material is all that can be made out in these positions.

($\times 300$).—The granular material along the course of the vessels and around the Malpighian bodies is seen to be composed of small round cells, which appear to be largely the result of inflammatory migration of polymorpho-nuclear leucocytes—some of these appear to be pus cells—but partly of active proliferation of the connective tissue cells. In many cases the cellular mass has fallen away from its position, leaving a small cavity, whilst in the more acute forms these cavities communicate with one another. In a section of the true surgical kidney, stained by Gram's method, staphylococci may be distinctly seen. Note too that these cocci may sometimes be seen in the tubules, the epithelium of which is undergoing marked fatty degenerative changes; there may be no regular catarrh in these tubules, although in the early stages cloudy swelling of the epithelium is invariably present.

302. In a second form of suppurative nephritis, frequently associated with ulcerative endocarditis, there can be no doubt that the multiple abscesses result from the impaction of septic emboli in the interlobular vessels, and in the intertubular and intra-glomerular capillaries. These emboli consist of scraps of fibrinous lymph in which are embedded micrococci, which latter multiply rapidly and set up abscess formation as already described (§ 229), as, in addition to the condition above described, masses of deeply stained micrococci may be found in all these positions (in a section stained with methylanilin-violet).

Under certain conditions nephritic abscesses become more chronic, in which case large caseous masses, encapsuled by firm fibrous tissue, may be met with. On microscopic examination, the tissue around

is found to be atrophied, whilst chronic interstitial inflammatory changes are also met with. (See § 298 *et seq.*)



FIG. 124.—Section of kidney from a case of acute septic embolic nephritis, miliary abscess around septic emboli of intertubular and glomerular vessels. Gram and alum hæmatein and picro-erythrosin. ($\times 300$.)

- a.a.* Masses of micrococci in an afferent arteriole at the entrance to a glomerulus, septic embolism.
- c.* Masses of micrococci in intertubular capillary.
- h.* Small hæmorrhage.
- l.c.* Polymorpho-nuclear leucocytes in a commencing abscess.
- c.t.* Epithelium of convoluted tubules, cloudy swelling.
- b.* Endothelium lining Bowman's capsule.
- t.* Glomerular tuft with covering epithelium.

INFARCTION

303. Embolic infarcts, the result of the impaction of emboli,—detached fragments of fibrin, or young “vegetations,” usually from the

left side of the heart,—may be met with in all stages of development, from the swollen, red, conical, or wedge shaped patch in the cortex, or the dense, pale-veined area, surrounded by a hyperæmic zone, to the caseous mass or cyst surrounded by a fibrous capsule, or the simple, puckered, and retracted scar which marks the position of the old infarction. In the kidney infarcts are usually pale, except at the periphery, where there is frequently a distinct red zone in which the blood vessels appear to be distended, and in which, too, there appears to be some inflammatory reaction. In the cortex the infarction may be red with very faint brownish or brownish-yellow mottling throughout. These infarctions are usually multiple and comparatively small. So marked may this be that the scarred kidney may look almost like a granular contracted kidney. Harden (§ 63 or 64), stain (§§ 103 or 104 and 122).

($\times 20$).—The specimen under examination taken from a tuberculous kidney had in its substance a series of very recent infarctions. In one of these the epithelial cells of the tubules and the Malpighian bodies take on all nuclear stains badly—they are practically dead. The swollen protoplasm of the epithelial cells is reddish-brown, and the nuclei have entirely disappeared. In the connective tissue and immediately around some of the pre-existing blood vessels the nuclei still retain their staining capacity, this indicating that the process is of comparatively recent date. Around the dead area a number of the blood vessels are congested, and here and there we have evidence of emigration of the polymorpho-nuclear leucocytes, but, as yet, no proliferation of the connective tissue cells. Later the emigration of leucocytes becomes still more marked, and there is some proliferation of connective tissue cells at the margin of the dead mass.

($\times 300$).—These points are made out much more distinctly. Note that in the area of dead tissue the blood vessels are practically empty except at the extreme margin; hence the ischæmic character of the infarction, except at the margin where the vessels are distended and there is commencing inflammatory reaction.

($\times 90$).—In a section from the margin of a wedge-shaped infarction in the medulla of older standing, the epithelium in the tubules has undergone marked degenerative changes, and in many cases has almost entirely disappeared, being now represented merely by colloid and pigmented casts. It is sometimes difficult to distinguish between the original blood vessels and the tubules, as many

of the tubules now contain altered blood corpuscles and leucocytes

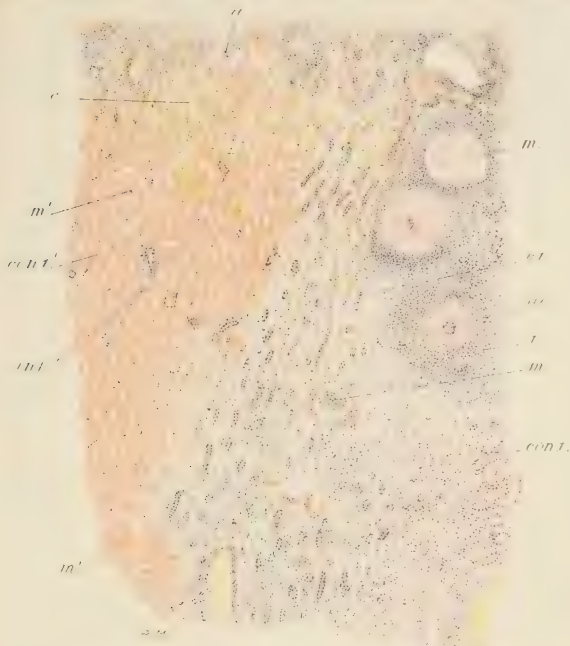


FIG. 125. Infarct in the cortex of a tuberculous kidney. Stained with alum hæmatein and picro-erythrosin.

- a.* Capsule and tissue immediately underneath it nourished by the capsular branches of the renal arterial system.
- c.* Zone of congestion around the infarcted area.
- inf.* Infarcted area containing cells, etc., which no longer take on the nuclear stain. This tissue, *con.t.* convoluted tubules, *m'.m'*. Malpighian bodies, is "dead." The nuclei of the more resistant and less organised tissue, connective tissue, and epithelium of the collecting tubules are still stained.
- m.m.* Malpighian bodies, *con.t.* convoluted tubules, and *c.t.* collecting tubules outside the infarcted area.
- g.c.* Giant cell surrounded by early caseating zone and outside this is the
- t.* Cellular and reticular tissue.

that have taken up a considerable quantity of blood pigments. The

fibrillar tissue and basement membranes are considerably swollen and in the specimen under examination take on a deep pink stain from the van Gieson mixture, the dead cells, casts, and blood taking on the picric acid stain. In the red zone of the infarct at the periphery a number of red blood corpuscles may be seen lying in the connective tissue between the tubules and around the blood vessels.

DILATATION OF THE PELVIS AND CALYCES OF THE KIDNEY

304. Dilatation of the pelvis and calyces of the kidney may be due (1) to tubercular thickening of the walls of the ureter; (2) to obstruction of the ureter during the course of abscess of the kidney. This may be due (*a*) to the presence of a calculus in the ureter,¹ or (*b*)

¹ Forms of Renal Calculi—

- (1) Reddish or brownish-yellow uric acid calculi, in the form of gravel or rounded smooth masses, the size of a pea, or larger. These occur in great numbers, and are composed of uric acid mixed with urate of sodium or other alkaline urates.
- (2) Calculi filling the pelvis and calyces of the kidney, irregular and branching, with a somewhat rough surface, and composed of phosphates and uric acid or urates.
- (3) Oxalate of lime calculi, small, smooth, or mulberry masses, dark grey or purple in colour, and extremely hard. Soluble in the mineral acids.
- (4) Carbonate of lime calculi are found in the kidneys of old people. When pure they are usually yellow and hard. Carbonate of lime, like the following, enters into the composition of many of the other forms of calculi.
- (5) Phosphate of lime calculi are met with as small, smooth, faceted, nodular masses, usually much whiter, softer, and more friable than the calcium carbonate calculi.
- (6) Triple phosphate of ammonium and magnesium may be found deposited on any of the various other forms of calculi, or on an inflamed surface, especially where there is decomposition of the urine. It forms a soft grey or dirty white layer, and when examined under the microscope is found to be made up, principally, of the characteristic "knife-rest" crystals.
- (7) Cystin calculi are rarely met with. They are light yellow, ovoid, crystalline masses, soluble in ammonia. From the solution so made the crystals may be obtained in the form of hexagonal plates by evaporation.
- (8) Xanthin calculi are also occasionally, but very rarely, met with as white waxy-looking masses. They are soluble in hot nitric acid. When the solution is evaporated, and the residue heated with caustic potash, "a beautiful violet-red colour" is obtained.
- (9) Bile pigment calculi are sometimes met with in patients, especially new-born children suffering from icterus. The bile pigment is deposited in granules in the epithelium of the tubules, or it may form distinct calculi, composed of flakes of bile pigment or of crystals of bilirubin.

to the existence of some obstruction to the outflow of the urine from the bladder, accompanied by decomposition of the urine (stricture, enlarged prostate, and a dirty catheter). (3) Simple obstruction of the ureter, or of its orifice, or of the outlet from the bladder, by any of the above agencies, without the decomposition of the urine, may give rise to simple hydro-nephrosis, in which there is dilatation of the pelvis of the kidney with gradual atrophy of the papillæ from the pressure of the urine as it accumulates; the papillæ gradually disappear, and leave the interpyramidal cortex projecting to form septa. (See also § 300 (2).) Externally, the kidney presents a lobed appearance. Running down from the depressions are septa, more or less perfect, composed of membranous-looking fibrous tissue only. The cortex may be extremely thin and atrophied, and nothing may remain but a thin crust enclosing cavities of considerable size, which are usually filled with water and urinary salts. If the disease is of long standing, a mucous fluid, only, is found in these cavities.

RARER DISEASED CONDITIONS OF THE KIDNEY

305. *Syphilitic gummata* are very rarely met with. They are situated near the surface of the cortex, are of small size, and present all the characters of gummata in other organs.

Leucocythæmia.—Changes are sometimes met with in the kidney in this general condition. Both kidneys are affected, and are then considerably enlarged; each may weigh 14 oz. (400 grms.) or even more. The capsule strips off easily, leaving a pale grey, smooth, flabby surface, mottled with numerous grey or cream-coloured patches and minute hæmorrhages. On section, both cortex and medulla are enlarged; and it is often difficult to make out where one begins and the other ends. The cortex is pale, and, in addition to the smaller hæmorrhages, a few larger ones are occasionally met with. There may be a few small cysts present. The striation of the pink medullary pyramids is distinctly marked, and grey lines, with enlargements at intervals, alternate with red or pink streaks. In the boundary area the grey predominates, and here the medulla gradually merges into the cortex, from which, in this region, it is almost indistinguishable, except by the position of the larger vessels and the swelling of the medulla. The minute hæmorrhages are most numerous in this superficial portion of the medulla: here, too, the grey patches stand out most

prominently: there are frequently, however, numerous hæmorrhages at about the level of the looped tubules of Henle, and also in the mucous membrane of the pelvis.

Harden (§ 62 or 63), stain (§§ 102, 110 (*b*)), and mount (§ 195 or 199).

($\times 50$).—Along the lines of the intertubular capillaries, and within Bowman's capsule, also in the medulla between the straight tubules,

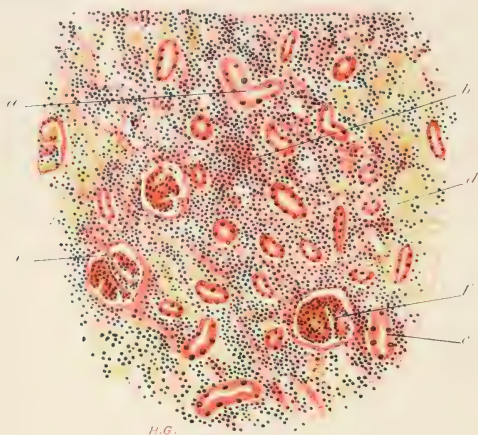


FIG. 126.—Section of kidney from a case of leucocythæmia. Stained with alum hæmatein and picro-erythrosin. ($\times 90$.)

- a.* Comparatively normal convoluted tubule.
- b.* Enormous numbers of leucocytes and myelocytes between the tubules.
- c.* Small vessels filled with leucocyte thrombi, and surrounded by leucocytes.
- d.* Hæmorrhagic mass of leucocytes around a tubule.
- e.* Hæmorrhagic mass of leucocytes at the point of entrance of an afferent arteriole.
- f.* Glomerulus in which are a few extra leucocytes.

The whole of the lymph spaces of the connective tissue are filled with leucocytes. In the greater part of the section there are no leucocytes in any of the tubules.

and even in some places in them, there is an enormous increase in the number of deeply stained nuclei. At intervals, too, they form small plugs in the blood vessels, and near these may be seen small hæmorrhages. The connective tissue spaces are simply crammed with

these nuclei. There may be a few fibrils of coagulated fibrin, but nothing else, between these cells.

($\times 300$).—The nuclei are those of leucocytes, often myelocytes, which have escaped along with a number of red blood corpuscles from the ruptured vessels. The hæmorrhages are, of course, composed very largely of leucocytes. The epithelium in the tubules may, in these cases, be comparatively healthy.

TUMOURS OF THE KIDNEY

306. Of primary tumours the following forms may be met with in the kidney :—

(1) *Lymphadenoma*. (See § 444.)

(2) *Lympho-sarcoma* and small round-celled sarcoma are usually congenital. They both lead to enormous enlargement of the organ; they are pale, and have numerous hæmorrhages scattered throughout. Spindle-celled sarcomas, in which, frequently, are a few fragments of striped muscle fibre, may also be found. They are very similar in appearance to other forms of sarcoma.

(3) *Fibroma* occurs as a firm hard nodule (§ 434) about the size of a millet seed, somewhat rounded or elongated in form, situated, usually, about the centre of the pyramids, but it may occur in almost any part of the kidney, its pelvis, or its capsule. Under the microscope it appears to be more cellular than are most fibromas; otherwise it corresponds to the description of a soft fibroma given in the section on Tumours (§ 434).

(4) *Non-striped muscular tumours*—*myomata* (§ 439)—are also found, usually near the apices of the papillæ.

(5) Simple *adenoma* (§ 448) has been described, but the malignant form is much more frequently met with. The former is said to begin in the collecting tubules. It appears as a small pale pink or grey mass about the size of a filbert. The epithelium lining the spaces is columnar and well formed, almost like renal epithelium.

(6) The malignant form of adenoma, which is really a cancer, usually begins in the cortex, where the growths are at first not very large; ultimately the whole organ appears to become infiltrated, when it may attain an enormous size. The typical structure of the kidney is lost, and we have in its place a large encephaloid pinkish mass, with yellowish and grey patches, and numerous softened hæmorrhagic patches, from

which blood and cancer tissue may make their way to the urine. The tissue, examined microscopically, resembles, very closely, the malignant adenoma already mentioned. (See § 470.) It is probable, however, that cancer of the kidney is by no means so common a condition as was formerly supposed, and that many so-called cancers are, in fact, vascular sarcomatous growths.

SECONDARY TUMOURS

307. The most common of these are the various forms of *cancer* and *sarcoma*, which may or may not attain considerable size. They are usually multiple. (See Chapter XIV.)

PARASITES

308. (1) Hydatid cysts of all sizes and in various stages of degeneration are met with, though comparatively rarely.

(2) In the mucous membrane of the pelvis of the kidney, especially in the veins, the matured *Bilharzia hæmatobia* is sometimes met with, in which case the ova may always be discovered in the urine.

(3) The *Filaria sanguinis hominis* occurs in the kidney, and has been found in the urine during life in cases of chyluria.

(4) A few instances of the presence of other parasites in the kidney, such as *Cysticercus cellulosæ*, *Eustrongylus gigas*, and *Pentastoma denticulatum*, have been recorded, but such cases are of extremely rare occurrence. (See Chapter XV.)

CHAPTER VIII

THE LUNG

309. In order that the various morbid processes in the lung may be understood, and that the appearances presented by the tissues of the lung in disease may be interpreted aright, it is necessary first to examine the healthy organ, and to describe, briefly, its structure.

Naked-eye appearances.—The lung, when taken from the male body in the normal condition, should weigh about $1\frac{1}{2}$ lb. (680 grms.), from the female 1 lb. (450 grms.). It is enclosed within a fibrous sac or capsule, the outer surface of which is smooth, glistening, serous. In people who live in the country, the lung has a pink colour (Shetlander's lung); but in the lungs taken from the inhabitants of towns the pink colour is replaced by a dull bluish or pinkish-grey, with a series of darker streaks (carbon pigment) outlining the lobules. A healthy lung crepitates under the finger. On section a quantity of blood, mixed with air, may be squeezed out; a fresh section presents a bluish-purple, and not a bright arterial red colour (though this makes its appearance when the cut surface is exposed to the air for a short time). The open bronchi contain only a small quantity of frothy mucus, covering a mucous surface thrown into longitudinal wrinkles.

The lung may be compared to a bunch of grapes, the stalks being the bronchi and the grapes the air vesicles. These bronchi divide regularly and dichotomously, but the division of the two largest bronchi takes place in a different manner in the two lungs. The left bronchus runs for some distance before dividing, and then one branch goes to the upper, and the other to the lower lobe. The right bronchus divides almost immediately into two branches, the lower of which goes to the lower lobe of the lung, whilst the upper one is subdivided, the lower branch going to the middle lobe and the upper one to the upper lobe. These bronchi divide and subdivide until they come down to the smallest or terminal bronchi,

each of which has around it a system of bronchioles and air vesicles, all communicating with it, and together forming what is known as a lobule. Accompanying the bronchi, at the root of the lung, and passing into the organ along with them, is a mass of connective tissue, which supports a series of structures, to which reference will afterwards be made. On examining the pleural surface of the lung, it is found that this division into lobes and lobules is not at all an artificial one, the lobules being readily enough discerned as polygonal areas, each of which is bounded by a series of black lines. The air vesicles which form this lobule all communicate with a terminal bronchus. On section these black lines are found to represent bands of connective tissue (interlobular septa), from which finer septa run between the smaller groups of air vesicles. These form a strong supporting network of connective tissue, the large bands of which are situated at the root of the lung running along the bronchi, where they are met by the prolongation of a strong fibrous covering to the lung, composed of bands of considerable size, which run into the substance of the organ. (See Fig. 128.)

This connective tissue framework, as in other organs, not only supports the characteristic epithelial structure of the lung, but serves also as a medium in which the blood vessels, nerves, and lymphatic vessels and spaces may ramify before they come into direct relation with the alveoli or air vesicles.

In order to understand the openings in the tissue which may be seen in any specimen of normal lung under a low power, it will be well to describe the structure of one of these lobules, as this structure has a very important bearing on the formation of cavities in certain diseases, such as emphysema and phthisis. When the terminal bronchi, or the last branches resulting from the dichotomous division of the bronchi, are reached, it is to be noted that numerous small branches, more or less at right angles to the terminal bronchus, or continuous with it at its termination, are given off (Fig. 128). These vary in number somewhat, but there appear to be at least six of them. Each of these divides into two branches, the terminal bronchioles. At the end of the terminal bronchiole is a tuft of two or three small tubes, each of which continues as such for a short distance, and then suddenly opens out into what is known as an alveolar passage. The walls of this alveolar passage are delicate, and are really made up of a series of air vesicles, which have

a somewhat different arrangement at different points. Along each side of the passage are larger pouches, which in turn consist of a series of air vesicles; between the openings of the pouches the air vesicles surround the alveolar passage, from which point they are continued as the walls of the larger pouches. At the end of the alveolar passage, similar large pouches also composed of a series



FIG. 127.—Drawing from fusible metal cast of the air cavities of a foetal lung, made and kindly lent by C. W. Cathcart. ($\times 30$.)

- a. Air sac or infundibulum.
- b. Atrium. Terminal bronchus, from which lateral branches are given off at right angles.
- a.f. } Alveolar passages, opening into which are the infundibula (I).
- a.p. }
- alv.d. Alveolar duct or terminal bronchiole.
- Res.br. Respiratory bronchiole.
- c. Small bronchus.

On the surface of some of the casts of the infundibula the markings corresponding to the septa of the air vesicles may be seen.

of air vesicles, are met with. The pouches at the sides are spoken of as the lateral infundibula, those at the end as the terminal infundibula. The *alveolar passages* in connection with a *terminal bronchiole*, with their *infundibula* and *air vesicles*, make up a *lobule* or *acinus*, whilst the whole of the acini in connection with a *terminal bronchus* make up a single *lobule*, the base of which is seen on the

surface of the lung, as the polygonal area surrounded by the dark pigmented connective tissue. Supporting the walls of these various cavities is the *connective tissue*, first of all between the various lobules, as the interlobular septa; also as prolongations from the peribronchial connective tissue, running towards the centre of the lobule, and from the centre to meet that from the periphery derived from the pleural sac and the interlobular septa. There is thus formed a network of connective tissue which supports the blood vessels and nerves of the lung, and in which are the lymphatics and lymph spaces.

Alongside the larger bronchi, embedded in the peribronchial tissue, run not only the large pulmonary artery and vein, but also the smaller bronchial vessels (see Fig. 128); with the smaller bronchi, however, only the pulmonary artery runs, the pulmonary vein being situated at the periphery of the lobule, so that, on making a section through a larger bronchus and its accompanying vessels, three openings of considerable size are seen lying side by side; whilst on making a section through one of the terminal bronchi, only two openings are seen together—the bronchus and the pulmonary artery, the third opening—the pulmonary vein—being situated some little distance away.

Harden a section of healthy lung (§ 62, 63, or 64), stain (§ 102, 103, or 104), and mount (§§ 195 or 193 and 199).

($\times 50$).—Note (1) the pleura at one margin of the section—the smooth surface; (2) the interlobular septa; (3) the bronchi with their accompanying vessels; and (4) the air chambers, into which these bronchi open.

($\times 300$).—(a) The *pleura* is seen to be divided into two distinct layers—(1) the superficial, seldom pigmented, and (2) the deep layer. Covering the superficial layer, in very carefully made preparations, may be seen a layer of endothelial cells—large flattened nucleated cells—which, seen in a section taken from a fully expanded lung, are spindle-shaped. Both layers of the pleura are made up of fibrous (pink) and elastic (yellow) tissue arranged in bundles. The superficial layer contains a number of blood vessels and a very complicated network of delicate yellow elastic fibres, which are well brought out by Weigert's elastic fibre stain (§ 167), whilst between the bundles are numerous small plasma spaces or lymphatics. Between the lymphatics of the superficial and deep layers there is not a free communication, but those of the superficial layer communicate freely with the pleural cavity.

Beneath the superficial layer of the pleura is a delicate elastic layer

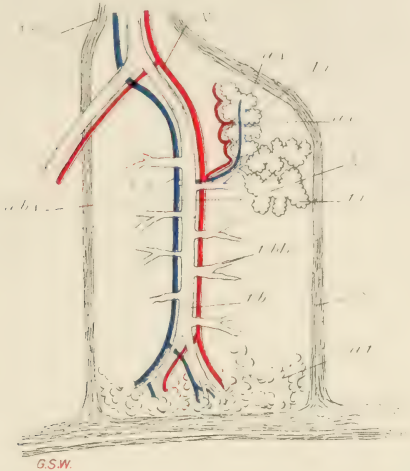


FIG. 128.—Diagram of a lobule of the lung, somewhat exaggerated as regards the number of terminal air sacs. Fig. 127 gives the proper relation of the various parts.

- a.b.v.* Line of section where artery, bronchus, and vein are cut across.
 - a.c.* Line of section where the artery is placed at some little distance from the vein.
 - t.b.* Terminal bronchus.
 - t.bl.* Terminal bronchiole, from which open the small alveolar ducts.
 - A.P.* Alveolar passage.
 - l.i.* Lateral infundibulum.
 - t.i.* Terminal infundibulum.
 - a.v.* Air vesicles.
 - a.t.* Alveolar tissue near surface.
 - P.A.* Branch of pulmonary artery.
 - P.V.* Branch of pulmonary vein.
 - I.S.* Interlobular septum.
 - I.S.B.* Interlobular septum prolonged from peribronchial connective tissue.
 - D.P.* Deep layer of the pleura.
 - S.P.* Superficial layer of the pleura.
- The three alveolar passages constitute an acinus; the parts between the interlobular septa, a lobule.

which, in pleurisy, becomes swollen and very distinct; then comes the

deeper or subpleural layer, which is considerably thicker than the superficial layer, but which is made up of more areolar-looking fibro-connective tissue. It is freely supplied with blood vessels, some of them of considerable size (filled with greenish corpuscles). The lymphatics in this layer can be readily distinguished, as, even in the healthy lungs, they contain small quantities of carbon pigment.

Continuous with this more open subpleural layer, and of similar structure, are the interlobular septa, which send off small branches to support the parenchyma of the lung, and are prolonged to meet the connective tissue surrounding the bronchi, so that several bands of connective tissue are seen in direct continuity between the subpleural layer and the walls of one of the bronchi. In all these bands the lymphatic vessels and spaces are numerous.

(b) *The structure of the bronchi.*—($\times 300$).—(1) Lining the tube is a layer of *ciliated* epithelium, the cells of which are distinctly columnar in the larger bronchi, but are shorter, though still ciliated, in the smaller bronchi. A few of these are seen as goblet cells lying between the ciliated cells. (2) Between this, and at a lower level, are a number of ovoid cells, which appear to be imperfectly developed ciliated cells. (3) Still deeper is a layer of flattened cells, of which Debove's membrane is composed. (4) These cells rest on a delicate homogeneous layer or basement membrane (which stains pink (§ 102 or 103)), found only in the bronchus of man (Hamilton). This appears to play a very important part in bronchitis and bronchiectasis. It is very elastic, may be stretched to an enormous extent, and is not easily affected by reagents. (5) Beneath is a fibrous coat, in which are nuclei of connective tissue cells and a number of white blood corpuscles, whilst running through the tissue are a few yellow elastic fibres. (6) Then comes the muscular coat, made up of circular bands of non-striped muscle fibres, in which the rod-shaped nuclei may be readily distinguished. It is to the contraction of these fibres that the longitudinal folds described under the heading of *naked-eye appearances* are due. (7) External to this, again, comes the outer fibrous or connective tissue coat; in this are the bronchial cartilages (between which are the mucous glands, extending inwards), and the bronchial artery and vein, sections of which are seen. (8) Continuous with this outer fibrous coat are the interlobular septa. Around the smaller bronchi the quantity of yellow elastic tissue in the outer fibrous coat is considerable, but the glands and cartilages are fewer in number, becoming less numerous as the branches become smaller.

“The epithelium changes in character in the alveolar ducts; from columnar and ciliated it becomes cubical and non-ciliated, and there are patches of the respiratory epithelium . . . not only in the alveoli which beset the ducts, but also elsewhere in their wall. The plain muscular tissue of the bronchiole is continued on the walls of the alveolar ducts, but not on those of the atria, although some occurs around the mouths of the atria and even of the alveoli” (Schäfer).

(c) The terminal *air cavities* can best be seen in a silvered preparation (§ 137), say of the lung of a cat, but they can be made out in all healthy lungs.

($\times 50$).—Note the air cavities. Some of them are seen as small polygonal openings, bounded by a slightly tortuous line; on each side of this is a network of tortuous lines; resting on these lines are a few small round nuclei (of epithelial cells); other cavities with similar boundaries are considerably larger, and instead of being polygonal in shape, appear almost like the section of part of a racemose gland; others, again, are more or less rounded or ovoid, with a series of indentations along their walls. These correspond to sections through alveolar systems, infundibula, and air vesicles, and the student should make a careful study of these various openings, in order to be able to recognise the parts of which they are sections.

($\times 300$).—The irregular lines running at the margins of the air vesicles, or in the angles between the septa, represent blood vessels. The network of capillaries forms the floor of the air vesicle, and between its meshes are seen delicate bands of elastic fibre. Separating the blood vessels from the air are epithelial cells, of which there are two kinds: (1) More or less cubical cells, which are situated chiefly in the alveolar duct, or at the entrance to the alveolar passage, at the angles between adjacent infundibula and adjacent air vesicles, and a few, in groups, at intervals on the floor of the air vesicle; and (2) between these groups of small cells, large flattened cells, each of which has a rounded nucleus: the outline of each cell is marked out distinctly by the cement substance which is stained brown by the nitrate of silver. At intervals along the lines of cement are clear areas—the so-called stomata—which are apparently due to the heaping-up of cement substance at these points.

A complete air vesicle, then, is a cup-shaped cavity, lined with epithelium, either flattened or cubical, which rests on a fine network of capillary vessels. Supporting the capillaries is a delicate connective

tissue. These cups placed side by side form the walls of the pouches or infundibula, which are given off from the alveolar passages; they also make up the walls of the alveolar passages in the intervals between the infundibula. In the angles between these cups are larger vessels; the walls of the cups cut transversely appear as the outlines of the air vesicles.

ACUTE PNEUMONIA

310. Synonyms, "Common," "Lobar" (from the fact that, as a rule, the whole of one or more lobes becomes affected), "Sthenic" (from the type of the symptoms), "Fibrinous," "Exudative," or "Croupous" (because the exudation appears to be similar to that which forms the false membrane in croup—"Croupous" is not an appropriate name); and lastly, "Pleuro-Pneumonia" (as this form of pneumonia is almost invariably accompanied by pleurisy, with an exudation of fibrinous lymph on the pleural surface).

The process may be divided into four stages—

- 1st. Stage of congestion or engorgement, during which there are
(a) hyperæmia; (b) effusion.
- 2nd. Stage of red hepatisation.
- 3rd. Stage of grey hepatisation.
- 4th. Stage of resolution.

Only rarely does the lung come for examination in the early stages, when the changes which occur are characterised by the following appearances:—

STAGE OF CONGESTION

311. *Naked-eye appearances.*—In this stage, there is marked congestion of the vessels in the pleura at the base and posterior margins of the lung. Under the pleura small hæmorrhages are seen, and the substance of the lung is here somewhat firmer than it is towards the apices, but is not solidified, and does not sink in water. It is rather more friable than the normal lung tissue. On section, the surface is of a bright arterial red colour, owing to a retardation of the blood flow, in consequence of which the blood is longer in contact with the air, which still freely enters the lungs before death; it is owing to this retardation of the blood flow also that the tissue is somewhat œdematous. On pressure, a bright red or watery fluid mixed with air is forced

out; this fluid, examined under the microscope, is found to contain a considerable number of red blood corpuscles, but these appear to come directly from the blood vessels.

Harden (§ 62, 63, or 64), cut (§ 82 *et seq.*), stain (§ 102, 103, or 104), and mount (§§ 195 or 193 and 199).

($\times 50$).—A peculiar beaded appearance of the vessels bounding the air vesicles is observed. The capillary network is distinctly marked out, whilst in the space bounded by these vessels, a number of small nuclei (of the epithelial cells) may be discerned; similar nuclei are seen studding the beaded vessels.

($\times 300$).—The capillary vessels are distended with red blood



FIG. 129. Drawing of section of congested lung. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

- c.v.* Distended capillary vessels of vascular network in the wall of the air vesicle.
- e.e.* Detached epithelial cells.
- p.* Carbon pigment in perivascular lymphatics.
- v.* Small branch of pulmonary artery.

corpuscles, a few of which may have escaped into the air vesicles, where they may be recognised by their double outline and pale green

colour. The epithelial cells are swollen at some points, and at others are undergoing proliferation, or some of the large flattened cells are simply separated from the capillaries, and are lying free in the air space. Only here and there throughout the whole section is there any further effusion into the air spaces, but when this does occur, its characters are similar to those presented during the next stage; there may be slight hæmorrhages from ruptured capillaries. There comes a point, however, at which this effusion into the air vesicles becomes a very marked feature; and as soon as this is reached, and the material has coagulated, what is called the stage of red hepatisation is reached.

STAGE OF RED HEPATISATION

312. *Naked-eye appearances.*—The lung, or a lobe of the lung, has become solid, and now sinks in water; all the air vesicles are filled with a coagulated fibrinous effusion. As a rule, it is found that this solidification is confined to one of the lobes—the lower one—especially at its posterior portion. This arises from the fact that, as at first the effusion is fluid, it gravitates to the most dependent parts, where it undergoes coagulation changes. The affected portion is sharply marked off from the rest of the lung tissue, in which, however, there is, as a rule, marked congestion and œdema. Sometimes the whole of the organ may be hepatised, in which case the lung, instead of weighing about $1\frac{1}{2}$ lb. (680 grms.), may weigh 2 or 3 lb. (910 to 1630 grms.) or even more, in consequence of the large accumulation of exudation in the air cavities. Frequently there is considerable injection of the superficial vessels of the pleura, or there may be a layer of fibrinous lymph thrown out on its serous surface; in the later stages of the disease this evidence of pleurisy may invariably be met with. When handled, the lung feels somewhat firm, almost like a piece of leather, but it is so friable that the fingers may be made to meet in its substance much more readily than in a normal lung. On section, the tissue feels tough and elastic; but, as it is quite solid, it “cuts” readily, and does not give way before the knife. The cut surface is often compared to red granite, as it has a dull, or, after a time, a bright red, smooth, glistening appearance, mottled with paler and grey spots—older coagula; in some cases, this glistening gives way to a somewhat granular appearance, especially in the later stages, as the coagulum contracts slightly. On pressure, only a very small quantity of bloody serum exudes. The mucous membrane

of the bronchi is injected, and is covered with a layer of bloody, frothy, or viscid fluid. In the smaller bronchi small firm casts may be found, similar to those met with in the air vesicles.



FIG. 130.—Drawing of section of lung in a condition of acute pneumonia, stage of red hepatisation. Stained with alum hæmatein and picro-erythrosin. ($\times 60$.)

In the air cavities the delicate strands of fibrinous lymph and the cellular elements of which the coagula are composed are seen. The capillary blood vessels are distinguishable at places in the walls of the alveoli. Note the transparency of the clot, and that it does not take on the staining material at all readily. Observe also that the clot fills the air vesicle. The tunica adventitia of the small vessel seen in section is infiltrated with carbon pigment. *br*, bronchus.

Harden (§ 62 or 63), stain (§§ 102, 103, or 104, and 167), and mount (§§ 195 or 193 and 199).

($\times 50$). The air cavities are now completely *filled* with a delicate looking film, through which *light is readily transmitted*. In this film are seen numerous nuclei. The blood vessels forming the outlines of

the air vesicles are less distinctly seen than in the normal lung, and sometimes contain a comparatively small amount of blood.

The vessels in the deep layer of the pleura and in the interlobular septa are engorged with blood, and there is thickening of the fibrous tissue (due to œdema); on the surface, often above the flat cell layer, is a quantity of coagulated fibrinous lymph, which has all the char-

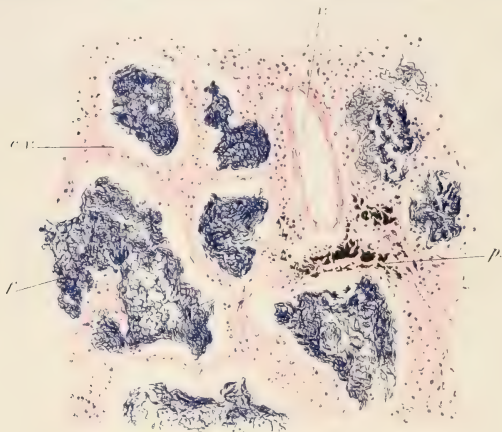


FIG. 131.—Drawing of series of air vesicles with contained fibrinous exudation. Red hepatisation. Weigert's fibrin stain and alum carmine. ($\times 90$.)

- c.v.* Blood vessels in interalveolar septa, in this case somewhat distended with blood.
- f.* Network of fibrinous lymph attached to the wall of the air vesicle; at some points it has retracted from the wall. The white and red blood corpuscles may be seen en:angled in the meshes of the fibrinous network.
- p.* Carbon pigment in perivascular lymph spaces.
- v.* Vessel with elastic tissue in its wall.

acters of that seen filling the air cavities and the smaller bronchi, except that it is stained somewhat more brown, is more granular, and is not quite so transparent.

($\times 300$).—The exudation completely fills, and even distends, the air vesicles; it is composed of a delicate meshwork of coagulated fibrin (exuded from the capillary vessels), the fibrils of which are attached to the walls of the air vesicle. Entangled in this meshwork

are—(1) numerous coloured blood corpuscles, again recognisable by their double outline and greenish colour; (2) a number of polymorpho-nuclear leucocytes with deeply stained nuclei; and (3) some larger (detached epithelial) cells with more delicately stained larger rounded nuclei. Sometimes larger groups of blood corpuscles, which have been poured out through ruptures in the walls of the vessels, may be seen.

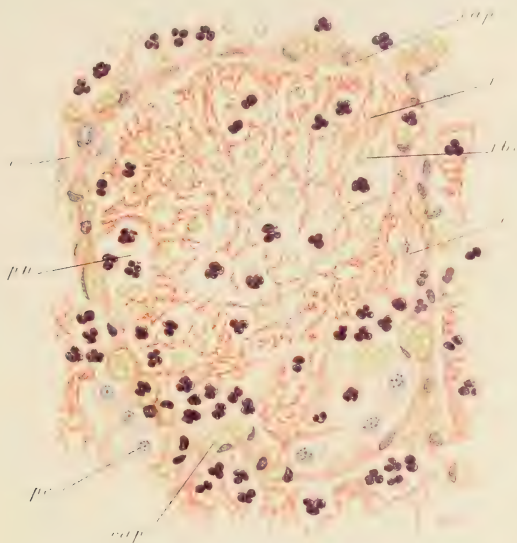


FIG. 132.—Drawing of section of lung—acute pneumonia. Red hepatisation. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

cap. Capillary vessel in alveolar wall.

e. Cell lining alveolus.

f. Fibrin network in which are entangled *p.c.* catarrhal cells, *p.n.* polymorpho-nuclear cells, and *r.b.c.* red blood corpuscles.

The more scattered corpuscles, as they have come through the walls of the vessels by diapedesis, have become entangled in the coagulum formed from the exuded blood elements.

The large nucleated cells, similar to those lining the air vesicles, are derived from the swollen and proliferating epithelial cells, or are simply flattened cells separated during the first stage of the process and

entangled in the fibrinous network ; the majority of these cells are near the wall of the air vesicle, though a solitary cell may be met with, here and there, throughout the network. Around the blood vessel is an exudation of leucocytes into the delicate connective tissue in the wall of the air vesicle, and there is probably, at the same time, a proliferation

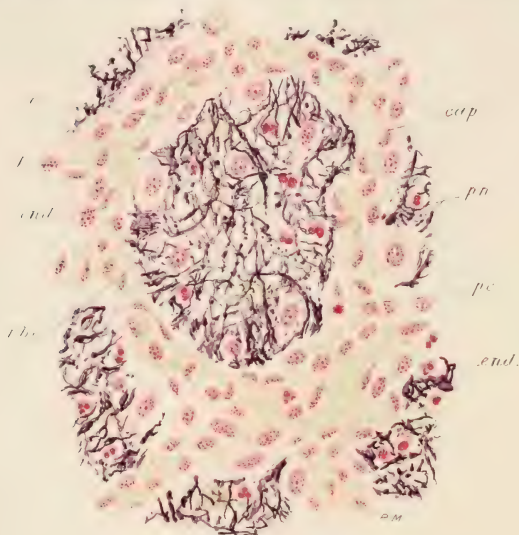


FIG. 133.—Section of lung from a case of acute pneumonia (due to inhalation of food). Stage of red hepatisation. Weigert's fibrin stain and alum carmine. ($\times 300$.)

cap. Capillary vessels in the thickened interalveolar wall.

end. Endothelial cell lining small blood vessel (vein).

e. Cell lining alveolar cavity.

p.c. Proliferating cell—catarrhal.

p.n. Polymorpho-nuclear leucocyte and (*r.b.c.*) red blood corpuscles entangled in (*f.*) meshes of fibrin.

of the connective tissue cells ; here, then, the first indication of an interstitial process, which in some pneumonias may become a very prominent feature, is met with. There is little difference in appearance between the hyaline leucocytes and the connective tissue cells. The exudation on the pleural surface is made up of similar elements—coagulated fibrin, red and white corpuscles, with, in some cases, a few

flattened cells derived from the endothelial layer which covers the pleura. In a section stained by Gram's method (§ 173), pneumococci or diplococci of pneumonia may be brought out. They are seen not only in the cells filling the alveoli and embedded in the mucin in that position, and in the lymphatics in the walls of the air vesicles, but also in the expectoration, especially during the early stages of the disease, when they are very numerous.

STAGE OF GREY HEPATISATION

313. *Naked-eye appearances.*—The lung is considerably heavier than normal. The exudation is found in the same positions as in red hepatisation. The affected part of the lung is solid, but does not appear engorged; frequently the lobe above that in which there is grey hepatisation is in the red stage, or is deeply congested. On the surface of the pleura a layer of coagulated lymph is invariably present. The tissue is heavy, firm, solid, sinks in water, "cuts" readily, and is extremely friable, breaking down very easily under pressure between the finger and thumb. The red colour has given place to a yellow or reddish-grey, or grey granite mottling. The cut surface is finely granular, an appearance very characteristic of this condition. The bronchi in this stage of the disease are usually somewhat congested. (This congestion is sometimes absent in the earlier red hepatisation stage.) Examine a scraping from the surface of the section ($\times 300$), and note that the yellowish particles which come away with the muco-purulent material consist of small casts of the air vesicles, alveolar passages, infundibula, or even of the small terminal bronchioles. On adding acetic acid to the masses mixed with water, there is a precipitation of mucin; and if some of the casts be treated with osmic acid ($\frac{1}{6}$ per cent. solution) for a few hours, teased out, exposed to the light, and mounted in Farrants's solution, they are stained black (fat); with picro-carmin or logwood they are also stained deeply. Harden (§ 62, 63, or 64), stain (§ 102 or 104), and mount (§§ 195 or 193 and 199).

($\times 50$).—The exudation in the air vesicles does not now completely fill them; it has shrunk, leaving a distinct interval between it and the wall: it is stained brick-red, and is granular and opaque, not allowing of the ready transmission of light to the eye, as in the red stage. The vessels apparently contain little blood, but are, neverthe-

less, distinctly seen. The pleura is thickened as in the stage of red hepatisation, and around the engorged blood vessels of the interlobular septa and the pleura a considerable number of deeply stained small round cells (leucocytes and young proliferated epithelial cells) are seen. On the pleural surface is a layer of coagulated fibrin, which is opaque, granular, and, with picro-carmin or picro-erythrosin, stained brick-red.

($\times 300$).—A mass of degenerated leucocytes may be observed



FIG. 134.—Section of lung; acute pneumonia. Grey hepatization. Stained with alum hæmatein and van Gieson's stain. ($\times 90$.)

- b.b.* Interlobular septum, in which small cell infiltration is well marked. (Early interstitial pneumonia.)
- c.* Thickened interalveolar septum.
- d.* Opaque, deeply stained, retracted clot in air vesicle. (Grey hepatization.)
- e.* Coagulum passing from red to grey stage, more translucent, and not so deeply stained. This occupies one of the larger terminal air cavities.
- p.e.* Increasing number of proliferating epithelial cells.
- p.n.* Increasing number of polymorpho-nuclear cells and small mononuclear cells, all of these are best seen on the margin of the retracting clot.

in each vesicle. The fibrin filaments are broken down and have become granular, and the red blood corpuscles have disappeared.

The polymorpho-nuclear leucocytes have become much more abundant, and are evidently undergoing degenerative changes, for they now appear to contain three or four nuclei, thus resembling pus corpuscles. The whole mass is separated from the wall of the air vesicle by a distinct interval, as noted above, and is brick-red, more or less granular, and obstructs the passage of light. Examine the wall, in which the vessel is somewhat compressed, and contains but little blood. Here are seen more of the polymorpho-nuclear leucocytes lying around the vessel, with a few lymphocytes and some young connective tissue cells becoming slightly elongated or spindle shaped. Young epithelial cells may also be seen on the wall of the cavity. Around the vessels in the interlobular septa, and in the pleura, are similar small round cells; whilst on the surface, in the deeply stained, opaque, granular-looking lymph, loops of blood vessels are frequently to be distinguished passing from the vessels of the pleura. The vessels in the peribronchial tissue are engorged, and surrounded by a number of leucocytes and young connective tissue cells.

In a section stained with osmic acid (§ 135) it may be seen that all the leucocytes are more or less fatty, and that between them are fatty granules and globules all stained black; in certain cases the lymphatics around the air vesicles are marked out by the black-stained fatty particles lying within them.

STAGE OF RESOLUTION

314. Naked-eye appearances.—In this stage the tissues are still pale, but they are softer and more flabby to the touch; a considerable quantity of a soft muco-purulent material may be squeezed out, and along with this small fatty casts of the air vesicles. Harden (§ 58, 62, or 63), stain (§§ 102, 103, or 104, 110 (*b*), and 135), and mount (§§ 195 or 193 and 199).

($\times 50$).—The granular mass in the air vesicle is much further removed from the walls than in grey hepatisation, is deeply stained, and the black particles and globules are much more numerous. The whole section is granular, and the blood vessels are more prominent.

($\times 300$).—The material in the air vesicles consists of fatty granules and globules, some of which have evidently been taken into the lymphatics around the air vesicles. The blood vessels contain numerous red blood corpuscles as they are again opening up. New

epithelial cells cover the capillary network, taking the place of those which were shed; they appear to be derived from the small cubical cells which have already been described (§ 309 (c)). The walls of the air vesicles are much more prominent during this stage, owing to the distension of the lymphatics, the return of the blood to the capillary vessels, and the new formation of epithelium.

Other terminations of pneumonia may be—(a) death during one of the earlier stages; (b) abscess formation where the inflammatory condition is very acute; or (c) gangrene, where the blood supply is rapidly and completely cut off by the great amount of effusion into the air cavities, and where the irritant action of the micro-organisms (in septic conditions) is allowed full play. In this condition there is a characteristic sloughy appearance, and an intensely fetid odour.

BRONCHIAL CATARRH OR ACUTE BRONCHITIS

315. Bronchitis in adults is essentially a catarrhal inflammation of the larger and medium-sized bronchi, and is usually associated with a similar condition in the larynx. In children the capillary bronchi are specially affected, the disease then often spreading to the air vesicles, and giving rise to catarrhal or lobular pneumonia.

As an uncomplicated disease, acute bronchitis is seldom met with on the post-mortem table; it is usually associated with chronic bronchitis, with heart disease, with some of the various dust diseases of the lung, or with one of the acute specific fevers. In children it is most frequently met with as an accompaniment of, or sequel to, measles, whooping-cough, scarlatina, and similar conditions.

Naked-eye appearances.—The lung is congested, and on exposure of a section to the air for a few minutes assumes a bright red colour. In the bronchi there is redness and swelling of the mucous membrane, with evidence of increased secretion and exudation; at first the mucous surface is covered with a glairy, transparent, tough, mucous fluid; later this becomes a “yellow muco-purulent fluid which covers the surface of the mucous membrane, and can be pressed out in the form of a tough tenacious pellet.”¹ The adventitia of the bronchus is greyish-white; the intense injection of the mucous membrane is readily seen when the tenacious mucus is removed, there is also some swelling and œdema of the injected membrane. The smaller bronchi are

¹ D. J. Hamilton, “The Pathology of Bronchitis,” London, 1883, p. 26.

apparently in a similar condition, and may be filled with the muco-

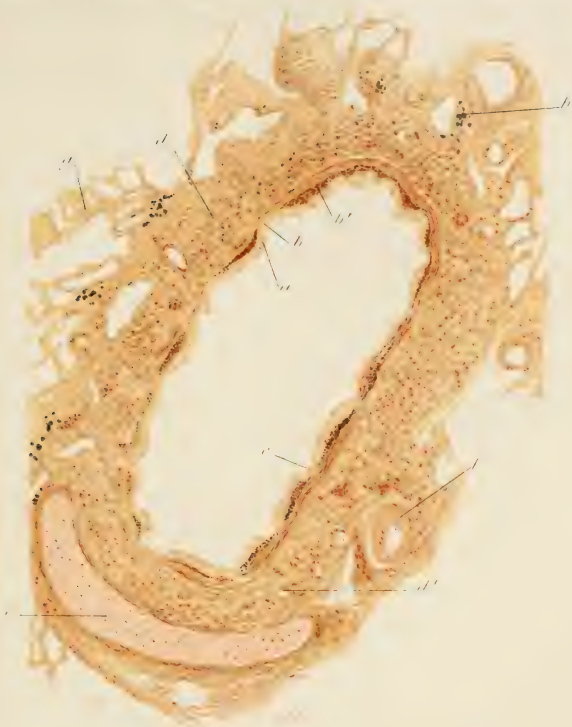


FIG. 135.—Section of a bronchus in which there is acute bronchitis.
Stained with picro-carmin. ($\times 50$.)

- a.* Single elongated cell resting on
- b.* The swollen and hyaline basement membrane. At other points the cells are more numerous, and are more rounded. *b'*. Submucosa thickened and pigmented.
- c.* Muscular coat of bronchial wall.
- d.* Adventitia of bronchus infiltrated with small round cells. In this may be seen the dilated vessels, *d'*.
- e.* Peribronchial cartilage.
- f.* Artery with thickened walls.
- g.* Lung tissue.
- h.* Carbon pigment in peribronchial lymphatics.

purulent secretion.

Harden a piece of lung in which are several of the larger bronchi (§§ 62 or 63 and 64), and a large thin section (§ 65), stain (§§ 103 and 110 (b)), and mount (§§ 193 and 199).

($\times 50$).—Next to the lumen is a layer of small round cells, with here and there one rather more elongated, generally placed at right angles to the surface of the mucous membrane. Beneath this is the basement membrane, which is enormously swollen, hyaline, and œdematous looking. Pushing their way for some distance into the basement membrane are distended blood vessels, which lie principally in the inner fibrous coat of the bronchus. Around the vessels, and separating the fibrous laminae, are numerous cells, seen as deeply stained granules. These are especially numerous around the vessels, but are to be met with throughout the greater part of this inner fibrous layer. The muscular coat may also contain a few of these cells, and the outer fibrous coat is often infiltrated with similar cells. This, which is evidence of peribronchitis, is usually not a very marked feature in acute bronchitis.

($\times 300$).—In a section taken from a case in which death has occurred within a few hours of the first attack, the blood vessels in the inner fibrous coat are distended, pushing their way into the basement membrane towards the lumen of the tubule. Later, in from sixteen to twenty-four hours, the basement membrane becomes swollen and œdematous, this change being followed almost immediately by a separation of the ciliated and columnar epithelium, which, on microscopic examination, may be found in the frothy expectoration. After this no columnar cells are again seen until the mucous membrane returns to the healthy condition. At this stage also there are marked changes in the mucous glands, the cells of which undergo cloudy swelling, and secrete mucus more actively, and the clear goblet-like cells are very numerous; in the centre of the gland there is a considerable amount of granular material. After a few days the typical catarrhal condition is reached. Lying on the swollen basement membrane are seen the flattened cells of Debove's layer, whilst above these are numerous rounded or pear-shaped cells, which are evidently derived by proliferation from the flattened cells. As these cells become detached, they, along with the mucus from the active glands, go to make up the muco-purulent discharge, the greyish parts being composed of mucus, the yellow or purulent material of the separated round cells. The changes in the inner fibrous coat are

chiefly around the blood vessels, which are distended with blood, and surrounded by a number of leucocytes and young connective tissue cells, all of which stain somewhat deeply with carmine and logwood. Extending into the muscular coat are similar round deeply



FIG. 136.—Portion of a section of the wall of a bronchus in a case of acute bronchitis. Stained with picro-carmine. ($\times 300$.)

- a.* Irregular columnar and rounded cells resting on
- b.* The swollen and hyaline basement membrane.
- c.* Submucosa infiltrated, and with small hæmorrhages in it.
- d.* Muscular layer of the wall of the bronchus, through which, at one point, the cells of the adventitia have made their way.
- e.* Peribronchial tissue (adventitia) in which are very numerous inflammatory cells (leucocytes and connective tissue). Here and there are small hæmorrhages (masses of cells stained green).
- f.* Dilated capillary.
- g.* Larger vessel, much distended.
- h.* Lung tissue.

stained cells, and it is to the presence of these cells, as a result of inflammation, that the weakening of the muscular coat, especially in the later stages, is due; for, as in the case of blood vessels, as soon as the muscular coat is involved, it gives way; there is dilatation of

the bronchus, and bronchiectasis results. The outer fibrous coat is usually involved only as the disease becomes more chronic and there is extreme cellular infiltration. In the medium-sized bronchi the changes are much the same, except that there are no mucous glands present, and consequently no mucus.

CHRONIC BRONCHITIS

316. This usually occurs in old people who have been subject to acute bronchitis during earlier life. It is often associated with emphysema, with valvular disease of the heart, in which there is venous engorgement and œdema, and with the interstitial pneumonias of various kinds.

Naked-eye appearances.—The most marked feature is emphysema; the air cavities of the free margins of the lungs are very much distended, and the other characters of this condition are readily recognised. (See § 319.) On cutting into the lung and squeezing it, a quantity of muco-purulent discharge is expelled from the cut ends of the bronchi; on examination under the microscope this is found to be composed principally of small round cells. Slit open a bronchus, and note that the mucous membrane is deeply congested, is usually of a dark red colour, is thrown into longitudinal folds, and is smooth and glistening; the mucous glands are often greatly enlarged, and may be seen as small glistening grey points, studding an injected or patchy surface. The smaller bronchi are usually dilated, and stand out more prominently than normal.

($\times 50$).—Note that the bronchial wall is greatly thickened and extremely granular, especially around the distended blood vessels, the cartilages are not so prominent as in the normal bronchus, and the muscular coat may be almost obscured. Lining the bronchus is a layer of rounded or pear-shaped cells, similar to those described in § 315. Columnar cells are seldom seen.

($\times 300$).—Examine first the epithelial cells lining the walls of the bronchus. They consist simply of rounded or incompletely developed columnar cells, and are very similar to those met with in the later stages of the acute form. The basement membrane is swollen, œdematous-looking, homogeneous, and hyaline, whilst its under surface is recessed at points by the pushing in of the vessels of the inner fibrous coat. These vessels never come to the surface of

the basement membrane. The small round cells in the inner fibrous coat vary slightly in size; the smaller ones are simply migrated leucocytes, but the larger ones are proliferated connective tissue cells and lymphocytes. These do not pass to the surface of the basement membrane, though a few may be found around the vessels in its deeper part. The cartilages and muscular fibres are shrivelled and atrophied as a result of the great increase in the number of the round, deeply stained, inflammatory cells.

In the outer fibrous coat, and following the interalveolar, and even the interlobular, septa, is a similar new cell formation; this, extending around the bronchi for some distance, may give rise to a kind of interstitial pneumonia. These changes are most marked along the lines of the bronchial vessels and lymphatics, extending from them to the lymphatics of the surrounding tissues.

CAPILLARY BRONCHITIS

317. Capillary bronchitis, or inflammation of the smaller, terminal or capillary bronchioles, is usually met with in broncho-pneumonia, and frequently follows the more acute form of bronchitis, not, probably, as the result of an extension of the inflammatory process, but rather of the application of the catarrhal products directly to the mucous membrane, or of the formation of a small plug of secretion in the bronchus. The changes are really those of bronchitis, peribronchitis, and catarrhal pneumonia combined,—accumulation of catarrhal cells in the bronchi, proliferation of the epithelium, swelling of the basement membrane, dilatation of the bronchus; the small cell infiltration of the peribronchial tissue extends to the interalveolar septa. Capillary bronchitis is so closely related to catarrhal pneumonia, that the other changes may be best studied under that head (§ 321).

EMPHYSEMA OF THE LUNG

318. As seen in chronic bronchitis and in old persons, emphysema is said to be atrophous, from the fact that in such cases there is often considerable wasting of the tissues of the walls of the air cavities; the emphysema met with in broncho-pneumonia along with collapse of patches of lung tissue is spoken of as compensatory, as some of the air cavities appear to be expanded to make up for the

“solidification” of others. Emphysema may also be classified as follows :—(1) Vesicular emphysema, in which there is simply dilatation of the larger air cavities, some of which appear to be expanded to compensate for others that contain no air as they are blocked with cells, etc. ; and (2) interstitial emphysema, in which the air has passed from the cavities in which it is normally contained into the surrounding or interstitial tissue. Of the latter form it is necessary to say little, except that to the naked eye the change is observed along the lines of the interlobular septa, in which a number of small clear air-filled spaces make their appearance. These spaces are never of any great size, but groups of them form beaded lines at the free margins of the lung under the pleura, or even between individual lobules. This form appears to be an extension of the vesicular process, and may be due (1) to rupture of air vesicles, or (2) to a wound in the larger air passages or in the pleura, the air escaping into the lymph spaces and gradually dissecting up the connective tissues.

VESICULAR EMPHYSEMA

319. Vesicular emphysema is usually met with where there is impaired nutrition of the lung tissue, which, when weakened, allows of the air cavities being more easily dilated. It is therefore specially common in chronic wasting diseases, in chronic lead poisoning, and in old people. In addition to these predisposing causes and conditions, however, there must be a direct or exciting cause, such as coughing as in the case of old people who suffer from chronic bronchitis. In the case of children the predisposing causes seldom play a very important part. Here whooping-cough is often the exciting cause ; there is forced expiration, with closure of the glottis during the act of coughing, which, when repeated and continued for some time, gives rise to well-marked emphysema. The causes, then, are long-continued and oft-repeated high pressure in the air cavities, especially when accompanied by weakening of their walls by impaired nutrition.

Naked-eye appearances.—On opening the chest cavity the lungs are found to be considerably more voluminous than normal, the anterior margins of the lung extending much further than they usually do—in some cases overlapping—when the sternum is removed. The lung may weigh several ounces less than in health. The whole of the outer surface has a deep red colour, except near the apex, down the

anterior margins, and around the margin at the base, where it is greyish-pink. In these areas the outlines of the lobules are not so distinctly visible, but when made out it is seen that the lobules are considerably increased in size. There is great distension of the lung tissue, and what are called emphysematous bullæ, in which the tissue appears to be light and spongy and feels almost like a mass of feathers in a silk bag, are formed. Squeeze the dilated portion, and observe that the air can be driven from one point to another along the margin of the lung; if a single incision be made, the air from the whole of the emphysematous portion may be driven out at the one opening.

On section, the tissue "cuts" with a peculiar gritty or rough feeling, and to the touch the cut surface is harsh and dry. The bullæ consist of large cavities, across which run thin non-vascular trabeculæ, evidently the remains of interalveolar septa. No blood oozes from the section where the bullæ are well marked. Throughout the whole of the non-emphysematous part of the section there is more blood than one meets with in the healthy lung; on pressure a yellow catarrhal fluid exudes from the bronchi, as in this condition there is usually bronchitis, often of long standing.

With a piece of string tie firmly one of the emphysematous bullæ, so as to keep in the air, and cut away behind the constriction. To the string attach a weight sufficient to sink the mass. Harden (§ 62 or 63), stain (§ 102, 103, or 104), and mount (§§ 195 or 193 and 199).

($\times 50$).—All the changes are most marked immediately under the pleura. Instead of the angular and polygonal openings of air cells, the openings are round, and are somewhat increased in transverse diameter. These rounded openings, however, are much fewer in number than are the polygonal openings in the healthy lung, in place of a number of which there are large irregular openings, usually surrounded by cup-shaped depressions. In a favourable section the capillary blood vessels are seen to form a network, with wider meshes than in the normal lung, and the transverse diameter of the vessel is not so great, the vessels, apparently, being stretched over an expanded surface. Although there is evident dilatation, and probably thinning of the walls, the thinning is not, at first sight, apparent, for the sections of the walls between the individual cavities are sometimes even broader than in the normal lung. This may be accounted for as follows: In emphysema the individual air cells are not distended; there is indeed a distension of the infundibula and the alveolar passages, and,

as a result of this distension, a flattening out of the air cells which

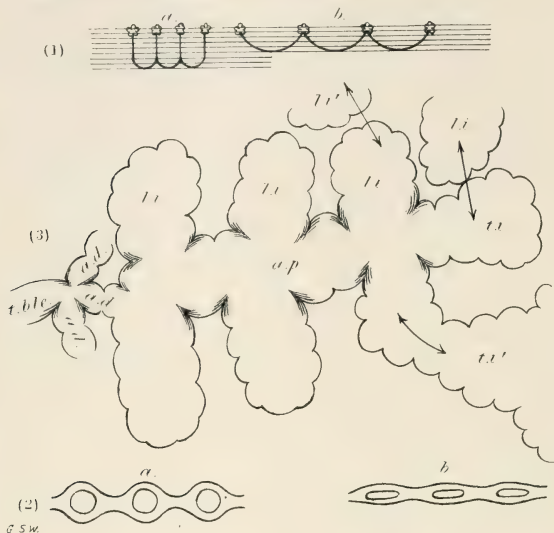


FIG. 137.—Series of diagrams illustrating the changes which take place in emphysema.

- (1) *a.* Normal air vesicles through which a series of imaginary sections are made at right angles to the wall.
b. Air vesicles flattened out. Sections pass obliquely through their walls, which therefore *appear* to be thicker.

- (2) *a.* Sections of capillaries in normal lung.
b. Sections of compressed capillaries in emphysematous lung. The pressure is due to the flattening out of the air vesicles.

- (3) *a, p.* Dilated alveolar passage.
 Infundibula, terminal *t, i*, and lateral *l, i*, dilated; air vesicles flattened.
t, i', Terminal, and *l, i'*, lateral infundibula of other alveolar passages into which ruptures, indicated by double arrows, take place; between *l, i*, and *l, i'* infundibula of the same alveolar passage, rupture may also occur.

t, b, c. Terminal bronchiole.

a, d., a, d., a, d. Alveolar ducts.

Hypertrophied muscular tissue at the mouths of infundibula, etc., is indicated by shading.

form their walls; the greater the distension of the larger cavities the

more marked becomes the flattening of the air cells, the walls of which also become considerably stretched. Consequently, if the normal air vesicle be imagined as represented by a cup with a thickened rim, the embryonic epithelial cells at the edge of the cup, forming this rim, the flattened-out emphysematous air vesicle may be compared to a saucer, also with a thickened rim. If the cup be cut down from above, a considerable number of sections—say eight or ten—are cut almost at right angles to the septa, and therefore in a direction showing least thickness of the wall. In cutting down the saucer, on the other hand, the number of sections must be fewer—only two or three—and each section passing obliquely through the wall appears thicker (though the wall may be actually thinned), and the relative, but not the absolute, number of sections through the bottoms of the concavities appears to be increased. Hence the apparent thickening of the walls of the spaces, and the numbers of membranous patches over which the capillary vessels are stretched. It will be remembered that when the section was made into the lung, there was, even on pressure, no exudation of blood from the emphysematous portion; this was due to the fact that the pressure on the vessels, and the stretching of them over an increased area, frequently bring about their occlusion. By this fact, too, is the absence of hæmorrhage after rupture of the septa during life accounted for. The breaking down of the septa follows a regular plan. The septa between individual air cells never give way, they are simply stretched out; but the septa between adjacent infundibula of the same alveolar system, or between infundibula of adjacent alveolar systems, are often broken down.

($\times 300$).—Verify all the above appearances, and note in addition a few fibres of muscular tissue around the openings of the infundibula. In emphysema, these fibres are more distinctly seen than in the normal lung, as they are somewhat hypertrophied. Besides the changes in the walls already noted, there are marked changes in the epithelium lining the air vesicles. It is granular and atrophied, and is evidently undergoing fatty degeneration. The atrophic changes are brought about by the cutting off of the blood supply through the constriction of the capillary blood vessels—the greater the constriction, the greater the amount of fatty degeneration and atrophy of the epithelial cells. Another change, due to the same cause, is thickening of the walls, and even atheroma, of the larger branches of the pulmonary artery. (See § 270.)

In this condition, owing to the obstruction to the passage of blood through the lungs, the right side of the heart has more work to do, may be dilated, and somewhat hypertrophied.

COLLAPSE OF THE LUNG

320. Collapse is met with under three or four different conditions.

(1) In patients who, before death, have been extremely exhausted, and have not had sufficient strength left to take a full inspiration. In such cases the collapse is in the lower and posterior, or least movable, portions of the lung. The tissue has a firm and fleshy feeling, is non-vesicular, and sinks in water. There is usually congestion of the collapsed and surrounding parts, and eventually the alveolar walls, at first merely in apposition, become adherent.

(2) In weakly new-born children it occurs in conoidal patches of one or more lobules at the periphery, especially near the root and at the base of the lung, and is known as *atelectasis* or *apneumotosis*. The collapsed patches are of a bluish or slate colour, and the tissue is so solid that it sinks in water. We have, here, *imperfect expansion*, due to pressure on, or to blocking of, the bronchus leading to a lobule or group of lobules.

(3) Where there is an effusion of fluid into the pleural cavity, as in pleurisy, there may be collapse of the whole lung. This may disappear if the fluid is absorbed; but where at the same time there is a thickening of the pleura, and organisation is taking place in the lymph, the lung may be bound down to the postero-internal wall of the pleural cavity, and the collapse remains. The lung is anæmic, though it may be somewhat œdematous. Spinal curvature, aortic aneurism, or distension of the pericardium, may bring about similar results.

(4) Collapse may be due to a wound in the chest wall, when the visceral pleura is also involved. Here the lung is first congested and solid, but after a time it may become more anæmic than the other lung, which, however, in such circumstances, has a tendency to become congested and sometimes emphysematous.

In all the above forms the tissue feels firm and fleshy, there is no crepitation, and no air can be squeezed out on pressure; a part of the solid lung will sink in water, and, though in the earlier stages of

collapse the lung is congested, in the later stages it becomes anæmic, as its function is left more and more in abeyance.



FIG. 138.—Section of the lung showing pleurisy and collapse. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- a. Layer of fibrinous lymph on surface of
- b. Pleura of which there is some thickening and in which blood vessels are dilated.
- c. Lung tissue in which the vesicles are collapsed, and the blood vessels congested. Much pigment in perivascular lymphatics.
- d. Wall of large blood vessel.
- e. Wall of bronchus.

(5) *Lobular* collapse takes place in broncho-pneumonia (§§ 318 and 321) as leaden-looking patches, each consisting of a lobule, or of a group

of lobules, frequently depressed below the surface of the surrounding lung. This form of collapse is said to be determined by a plug of mucus which acts as a ball valve, allowing air to pass out, but falling back to the mouth of one of the smaller openings at the bifurcation of a bronchus at every inspiration. Here, however, it must be remembered that even though the plug were fixed, the air in the vesicles could be absorbed and collapse would take place. This is accompanied by congestion of the capillary vessels of the collapsed parts, and by emphysema of the lobule supplied by the corresponding smaller branch of the bronchus, which is not plugged, and of the air vesicles immediately around it; in such cases there is often a distinct ring of distended air cavities around the collapsed area. This is usually situated at the base and posterior border of the lung, or along the free margins, but the depressed patches may be present at almost any part of the surface.

CATARRHAL PNEUMONIA

321. Synonyms, "Broncho" Pneumonia, "Lobular" Pneumonia. This condition, in its simplest and most typical forms, is met with in children who have suffered from capillary bronchitis (§ 317), during the course of some of the exanthematous fevers, or whooping-cough. It is also met with in hypostatic pneumonias, where the contents of the alveoli are to a great extent catarrhal, though the distribution of the process is then not necessarily lobular. During the earliest stage of catarrhal pneumonia, there is seldom any extensive pleurisy; in this respect it differs from the lobar form, in which pleurisy is a well-marked feature. On the surface of the lung, which usually appears somewhat congested, are seen a number of firm, solid, purple patches, varying in diameter from one-tenth to one-fifth of an inch. These are angular, and are frequently retracted slightly below the surrounding surface (collapsed lobules, § 320 (5)). In addition to these, there are a number of patches of similar appearance and consistence, which usually project beyond the surrounding surface (pneumonic patches). Around each of these the interlobular septa may be readily distinguished; the lobules in the immediate neighbourhood appear to be distended with air, and in some instances there is marked emphysema.

On section, the lung is found to be congested throughout; the small angular patches coincide in extent with the lobules, and near the

surface they are of a pyramidal shape; the solid patches are not very sharply defined from the surrounding tissue, are smooth and non-vesicular, and very little fluid can be squeezed from them; the walls of the surrounding dilated air vesicles evidently contain a considerable amount of blood, as the tissue appears very congested, and both blood and air may be squeezed out from these vesicles in considerable quantities.

During this stage, or more frequently during the next, the solidified and purple pneumonic patches may run together, and so form a solid mass with irregular outline, involving a considerable part of a lobe of the lung. A careful examination in such a case, however, enables one to say at once that this is not a condition of acute or lobar pneumonia. In addition to the irregularity of the outline, there are usually a number of lobules and smaller patches which have as yet not become fused into the main mass. Between the solid-looking patches, which are not granular, the lung tissue, though deeply congested, is otherwise normal.

The mucous membrane of the larger bronchi is deeply congested, whilst in the smaller branches there is acute catarrh; on squeezing (§ 312) a quantity of muco-purulent material is pressed out from them.

Harden (§ 62 or 63), cut (§ 82 *et seq.*), stain (§§ 103 or 104 and 110 (b)), and mount (§§ 193 and 199).

($\times 50$).—Examine a single lobule in which the catarrhal pneumonic process has been detected with the naked eye. It may be divided into three zones. In the centre is the small bronchus, recognised as a large rounded tube, with thickened granular-looking walls. In it there are usually a number of small cells, seen as small granules. Near the bronchus runs the branch of the pulmonary artery, known by the thickness of the adventitia and the quantity of pigment deposited in its lymph spaces.

In the narrow area immediately around the bronchus, the air vesicles are filled with a semi-transparent mass of delicate fibrils and cells, which differs from the exudation in the red hepatisation stage of acute lobar pneumonia only in the fact that it contains a greater number of cells. Where this process is not of long standing, the walls of the alveoli are thickened owing to the distension of the capillaries; near these capillaries a number of larger cells are usually found within the air vesicle. Outside this narrow zone the air vesicles are filled with catarrhal cells, with little or no fibrin between them.

These, or their nuclei, are deeply stained, and the mass is not nearly so transparent as is the exudation in the central zone. Here, too, the capillaries in the walls of the air vesicles are distended. The catarrhal change may extend to the periphery of the lobule, but in

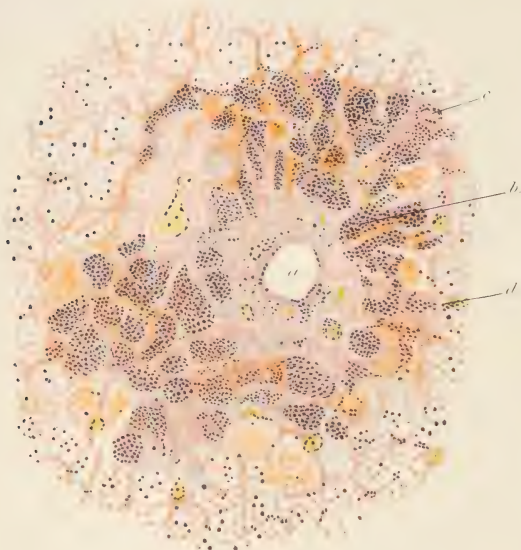


FIG. 139.—Section of lung; catarrhal pneumonia. Stained with alum haematein and picro-erythrosin. ($\times 90$.)

- a.* Section of small bronchus with infiltrated and congested walls.
- b.* Central zone of air vesicles filled with cells, wall of vesicles thickened, catarrhal cells, leucocytes, and fibrin all well marked.
- c.* Infiltrated interlobular septum, in which are distended blood vessels, *d.*

The catarrhal proliferation is best seen in the air vesicles around the more solid patch.

many cases there is an outer zone in which there is merely congestion of the capillary vessels, accompanied by slight proliferation or detachment of some of the alveolar epithelial cells.

Examine the interlobular septa, and observe that they are more prominent than normal, are swollen, and that the vessels in them are

considerably distended; around the vessels small polymorpho-nuclear leucocytes and hyaline (young connective tissue) cells are frequently seen. The deep layer of the pleura is in a similar condition and in it small hæmorrhages composed of red blood corpuscles are seen. There is some bronchitis (see § 315).

($\times 300$).—The plug of muco-purulent material in the lumen of the bronchus is composed principally of small “pus-like” cells; in which, on the addition of acetic acid to a fresh section, several small nuclei appear. The epithelium of the bronchus is proliferating, and is usually seen as a layer of irregular or flattened cells lying on the basement membrane; beneath this the vessels of the bronchial mucous membrane are distended; and around them, and in the peribronchial tissue, there is a great increase in the number of small round stained cells. This condition of infiltration with small round cells and thickening of the walls extends down to the minute bronchioles.

The air vesicles in the central zone are filled with fibrinous exudation; along with the clear unstained strands of fibrin numerous corpuscles, which differ considerably in size, are seen—(1) Red blood corpuscles; (2) granular corpuscles a little larger than the above, stained—polymorpho-nuclear leucocytes; and (3) rounded or oval cells, found in greatest numbers towards the periphery of the exudation. These are usually much larger (two to six times) than either of the preceding, and are made up of delicately stained granular protoplasm, in which one or more nuclei stand out as deeply stained bodies; small granules of pigment may also be seen in this cytoplasm. The nuclei vary considerably in size, even in the same cell. Such cells are all derived from the epithelium lining the air vesicles by a process of catarrhal proliferation. Though most of them are lying free near the edge of the alveolus, some are still adherent to the wall, and seem to be in a state of active proliferation; many of them are still attached to the parent cells by thin bands of protoplasm, which act as peduncles until they are set free.

In the next zone the air vesicles contain only catarrhal cells with a small quantity of granular matrix (mucin, fat granules, and granular protoplasm); the coloured blood corpuscles and the fibrin appear to be absent. On the addition of acetic acid the mucin between the cells may be brought out more prominently, but it is always a difficult matter to differentiate this intercellular material. In the

very early stage of the catarrh, the proliferating process may be well seen in this intermediate zone: the cells lining the air vesicle are swollen, multinucleated, and in many cases dividing; and are seen

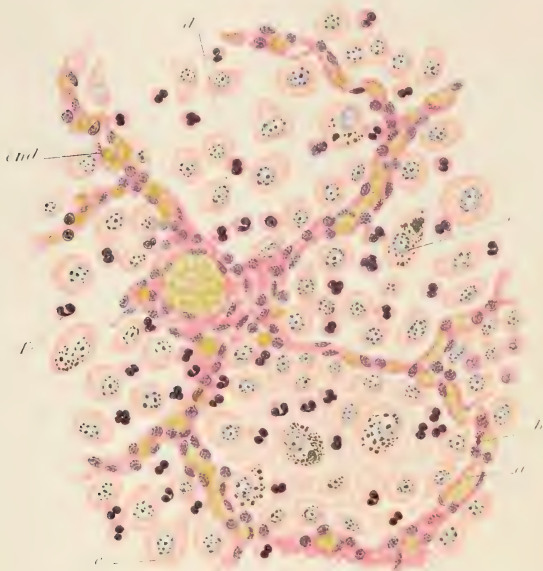


FIG. 140.—Catarrhal pneumonia; drawing of air vesicle. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

- a.* Congested capillaries in interalveolar septa.
- b.* Proliferating epithelial cells still attached to the interalveolar septa.
- c.* Pear-shaped cell held in position by a peduncle.
- d.* Catarrhal cells, lying free in the alveolus. Smaller groups in the adjacent alveoli. These large epithelial cells are quite distinct from the small cells seen in the exudation in acute pneumonia.
- e.* Large catarrhal cells containing granules of pigment.
- f.* Polymorpho-nuclear cells.
- end.* Endothelial cells lining the interalveolar capillaries.

in all stages of detachment from the alveolar wall. Where this is taking place the blood vessels are distended, and there is slight thickening of the alveolar wall, quite apart from the increased thickness of the epithelial layer. In what has been described as

the outer zone, this proliferative layer of epithelium and the distension of the blood vessels may be all that is seen, though in other cases the catarrhal products fill the cells at the margin of the lobule. It will be noted, even where the catarrhal process has been going on for a few days only, that the large detached epithelial cells are becoming more granular, less deeply stained, and are studded with small highly refractile bodies, which stain black with osmic acid (§ 135), showing that the cells are undergoing fatty degeneration. The interlobular septa, as already seen, are considerably thickened, the vessels running in them are distended with red blood corpuscles; there may be small extravasations around the vessels, and in addition there appears to be proliferation of the connective tissue cells, and a migration of polymorpho-nuclear leucocytes. The strands of fibrous tissue of which a septum is composed are somewhat separated from each other; and in the lymphatics, granular-looking masses of fibrin and cellular debris may be observed. The deeper layer of the pleura is usually in a similar condition.

The condition above described is the first stage of acute *lobular* pneumonia; but just as in the case of acute *lobar* pneumonia, the exuded and proliferated products may pass through a series of changes, as a result of which both the naked-eye and microscopic appearances are somewhat altered. In this form the various stages are described under the terms of red and grey splenisation and resolution, corresponding to the stages of red and grey hepatisation and resolution of the acute lobar form.

GREY SPLENISATION

322. Grey splenisation corresponds very closely to the grey hepatisation of acute pneumonia.

Naked-eye appearances.—The lung is not nearly so deeply congested as in the earlier stages, and in some cases it may appear, as a whole, even paler than normal, this being due to the pallor of the more solid patches. In the centre of each of the solid patches there is frequently a greyish point, or the grey colour may extend throughout the whole lobule. On palpation, the patches are not always firm and solid.

On section, note the slight congestion around the greyish-yellow lobules. On pressure, a quantity of muco-purulent material which,

on microscopic examination, is found to consist of pus corpuscles or of fat globules of various sizes, exudes from even the very small bronchi. On the addition of acetic acid, this material becomes stringy, owing to the precipitation of the mucin it contains. The mucous membrane of the bronchi is deeply congested.

Harden (§ 62 or 63), stain (§§ 103 or 104, 135, and 167), and mount (§§ 193 and 199).

($\times 50$).—The exudation in all the zones of the lobule is broken down, and in place of the catarrhal cells, smaller pus cells and large compound granular cells are seen in considerable numbers; these, when stained as above, are dirty brown and opaque, or stained with osmic acid are almost black—due to fatty degeneration.

($\times 300$).—The pus cells and compound granular (fatty) cells are very distinctly seen at the centre of the air vesicle; whilst at the margin there are usually a few small flattened epithelial cells growing, and forming a covering for the interalveolar septa. The other appearances are much the same as in grey hepatisation of lobar pneumonia (§ 310).

Later, the microscopic appearances are similar to those seen in the stage of resolution in acute pneumonia; the whole of the catarrhal products are broken down and softened; they form a fatty pultaceous mass, part of which is expectorated, and part absorbed by the lymphatics. In a section stained by osmic acid, the fatty material may be traced in the lymph spaces in the interalveolar and interlobular septa. The regenerated epithelium making its appearance at this stage is seen as a layer of cubical cells, gradually becoming more flattened, lining the air vesicle; in the interalveolar septa there is some increase in the number of fibroblasts.

As in the case of lobar or acute pneumonia, it is impossible to go into all the forms of disease which may follow acute catarrhal pneumonia, but the following more common sequelæ may be mentioned as referred to by several writers.

SEQUELÆ OF ACUTE CATARRHAL OR LOBULAR PNEUMONIA

323. (1) Acute suppurative broncho-pneumonia, the pneumonia being set up by retained bronchial secretion in which are numerous active micro-organisms. This condition is so acute, and the infiltration with polymorpho-nuclear leucocytes of the tissues around

the bronchus so great, and the digestive and destructive action of the micro-organisms so marked, that an abscess is formed, which may involve the whole of the tissue in the immediate neighbourhood of the bronchus. To the naked eye the lung presents the characteristic features of ordinary lobular pneumonia, with, here and there, points of suppuration.

(2) Chronic broncho-pneumonia appears to be little more than an interstitial pneumonia, set up by the irritation of the absorbed broncho-pneumonic products. It occurs as a diffuse form especially in children, and as a nodular form in old people. The appearances, both naked-eye and microscopic, are very similar to those of interstitial pneumonia (§ 327).

(3) Caseous broncho-pneumonia, of either the nodular or the diffuse form, was formerly classified as a true catarrhal pneumonia; now, however, it is referred to the tuberculous diseases, and will be described later (§ 332 *et seq.*).

(4) Owing to the changes in the walls of the bronchi in broncho-pneumonia, a form of ulcerative bronchiectasis (of the small lobular bronchi) is sometimes met with, in which we have the formation of irregular cavities containing softened or purulent material. This form is apt to be mistaken for caseous tubercle (Greenfield).

THE PNEUMONO-KONIOSES, OR THE DUST DISEASES OF THE LUNG

324. The most important of these are—

1. Anthracosis—Coal-miners' phthisis.
2. Siderosis—Needle-grinders' phthisis.
3. Silicosis—Stone-masons' phthisis.

Other forms are due to inhalation of vermilion, particles of wool, cotton, clay, or similar finely divided irritant dust particles.

Of these it will be necessary to examine specimens of the first and third only; in both of these, however, characters distinctive of the special disease or of the whole group may be observed.

“ANTHRACOSIS,” OR COAL-MINERS' PHTHISIS

325. This condition is the result of the inhalation of coal or carbon particles, which finding their way into the air passages, air vesicles, and

hence into the surrounding connective tissue, set up irritative changes, first catarrhal and then interstitial.

Naked-eye appearances.—The lungs of a coal-miner are deeply pigmented; they are increased in size, fill the *opened* pleural cavity more completely, and are heavier, much firmer, and more solid than normal. The pleural surface, at first sight, appears to be uniformly black, but on closer examination small dark spots, or accumulations of pigment, from which lines radiate in various directions may be seen, these lines corresponding to the lymphatics of the interlobular septa. Very frequently in the centre of these spots there is a lighter coloured point. Each of these spots, about the size of a mustard seed, or a little larger, with its light centre and dark periphery, is firm and fibroid.

On section, the lung is firm and tough; it has a peculiar harsh emphysematous feeling, whilst small nodules, similar to those seen on the pleural surface, but in smaller numbers, are scattered throughout its substance. Between the nodules the pigmentation is not nearly so well marked, though there is a considerable deepening of the colour of the tissue, especially along the course of the lymphatics of the interlobular septa. From the cut surface a large quantity of inky black fluid exudes; this in the fresh condition stains the hands. The bronchial glands when incised are indurated and deeply pigmented. The mucous membrane of the bronchi is pink or red (it is markedly injected)—not black. (The particles of carbon can gain no foothold, either because of the currents set up by the active cilia of the cells of the healthy epithelium, or of the active proliferation and secretion of mucus which occur on a catarrhal surface, the secretion washing away all foreign particles as they are deposited.)

At one or two points, if the disease be far advanced, the tissue presents the appearance of a solid black mass, or in the blackest part of such a mass there may be a ragged cavity bounded by sloughy looking walls.

Harden (§ 62 or 63), stain (§ 103, 104, or 106), and mount a section (§§ 193 and 199),—another, on which should be a piece of the pleura, and which should pass through several lobules,—unstained (§ 195).

($\times 50$).—The pleura is divided into two distinct layers, the more superficial of which is but slightly pigmented at any point, and is apparently little changed. Between it and the deep layer, which is sometimes three or four times the normal thickness, is a sharp line of demarcation. Throughout the thickened deep layer are black patches, which evidently follow the lines of the lymphatics, especially

around the blood vessels; these patches are sharply bounded by the walls of the lymph spaces or sinuses.

The interlobular septa continuous with the deep layer of the pleura are also considerably thickened, and their lymphatics are similarly injected with black pigment. From them the black lines and patches

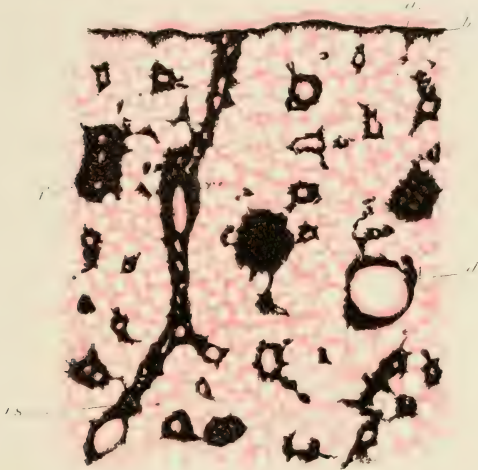


FIG. 141.—Section of coal-miners' lung, to show position of carbon pigment. Stained with alum carmine. ($\times 20$.)

- a.* Superficial layer of pleura, unpigmented.
- b.* Deep layer of pleura, in the lymphatics of which a large quantity of pigment has accumulated.
- i.s.* Interlobular septum, pigmented at margins. (In lymphatics of connective tissue.)
- f.* Small bronchi with thickened and pigmented walls.
- d.* Vessel with pigmented adventitia.

In all these pigmented areas there is great increase in the amount of connective tissue, so that each is hard and firm, and, from the amount of pigment that has accumulated in the lymph spaces, gritty.

may be traced into the perivascular and peribronchial tissue, as the peribronchial lymphatics are in direct communication with those in the septa, and thus with those in the deep layer of the pleura. The mucous membrane of the bronchus is entirely free from pigment of any kind, though it is frequently swollen and in a condition of catarrh (see § 315).

The interalveolar septa are thickened and pigmented ; the walls of the air vesicles are also thickened and studded with numerous dark-coloured patches. In the air vesicles coal particles are found in considerable numbers, some of them lying free on the surface of the epithelium, others contained within detached epithelial cells, whilst others again are found within swollen epithelial cells, still attached to the alveolar wall. In addition to these are numerous nucleated cells lying free in the cavity. In the lymphatics around the small branch of the pulmonary artery, the masses of carbon pigment are specially numerous. Here they act as irritant bodies and set up proliferation of the connective tissue cells, and so thickening of the adventitia or outer coat, fibrous nodules being formed around the vessel. Then endarteritis (§ 273) setting in, layer upon layer of proliferated cells (derived from the flattened cells of the intima lying directly in contact with the blood current) are formed until the lumen is narrowed, or in some cases obliterated, and only a solid fibrous nodule remains. Eventually this may undergo degenerative changes, soften and break down in the centre, leaving a small cavity bounded by ragged fibrous deeply pigmented walls. From the fact that the above changes are most marked where the nodules are most numerous, it appears probable that many of them must have an obliterated vessel in their centre, the process of degeneration being due to the obstruction to the lymph and blood flow.

($\times 300$).—Follow the course of the pigment in the lung. It is not found in the mucous membrane of the bronchi, which frequently, however, shows well-marked evidences of acute bronchitis (§ 315). In the air vesicles it is found in the different positions mentioned above ; the lymph spaces in the walls of the air vesicles are in many cases packed with it ; the connective tissue cells in the walls of these spaces, and some cells lying free in the lymph channels, are also pigmented. The cells in the air vesicles, as seen above, vary from the size of a polymorpho-nuclear leucocyte to three or four times that size, and some of them may have several nuclei. Occasionally, too, a few red blood corpuscles may be recognised.

There is evidently considerable proliferation of the connective tissue cells, nuclei are much more numerous than usual, and there is a great increase in the amount of fibrillated tissue around the capillary vessels, which are usually considerably dilated and distended with blood corpuscles. Small fibrous nodules are sometimes seen in the interalveolar septa. Similar changes, but on a more extensive

scale, are met with in the interlobular septa. The lymphatics contain pigment; there is a marked increase in the amount of interstitial connective tissue, many of the cells containing granules of carbon. The blood vessels may be distended, or, in some cases, the lumina, though filled with blood, are markedly contracted, owing to thickening of both the intima and the adventitia. In this position the fibrous nodules are pale and firm in the centre, but towards the periphery they contain, in the spaces between the bundles of fibrous tissue, a considerable quantity of pigment. From the alveoli near the surface the pigment is carried by the more superficial lymphatics of the interalveolar and interlobular septa to the deep layer of the pleura, and as seen above the thickening and pigmentation are both extremely well marked; all the changes observed in the interlobular septa are here repeated. The superficial layer of the pleura is usually unaffected; there is no marked pigmentation, and but little increase in thickness. The lymphatics of this layer do not appear to communicate with those of the subpleural layer.

From the lymphatics surrounding the alveoli nearer the root of the lung the pigment is carried to the perivascular and peribronchial lymphatics, giving rise to changes similar to those described in the above positions. Around the bronchi the changes are not so marked, but even here the fibrous tissue may be invaded, but never the mucous membrane proper.

To sum up: the small black nodules may be found in the interalveolar and interlobular septa, in the deep layer of the pleura, and in the perivascular and peribronchial tissue. Pigment is found in all these positions, and also in the air vesicles, either lying free or contained within the proliferating epithelial cells.

"SILICOSIS," OR STONE-MASONS' PHTHISIS

326. "*Lithicosis*," or "*Chalicosis*."—In essential details this process is similar to anthracosis; but all the changes are more marked and go on more rapidly, the particles of stone being much more irritating, give rise to greater proliferation of both epithelial and connective tissue cells, the catarrhal and fibroid changes are more extensive, and the changes in the vessels are more prominent, and appear to lead to greater destructive processes. In consequence of the fibroid changes, bronchiectatic cavities are here met with. The clinical history is that of ordinary phthisis, but the pathological process is quite distinctive. It is met with especially amongst stone-masons and quarrymen who

work in dry siliceous stone, the dust particles given off in the working of this stone being very fine and therefore readily inhaled.

Naked-eye appearances.—As soon as the hand is introduced into the pleural cavity, evidences of the disease present themselves. Over the surface are patches of adhesion in different stages of organisation, but most of them are exceedingly tough and fibroid, and it is often necessary to strip away the costal pleura before the lung can be removed. The pleura is, of course, much thickened.

The organ feels firm throughout, and the surface is studded with small, hard, fibrous nodules, about the size of a split pea (larger than those seen in anthracosis), which have a very characteristic appearance.

The centre of the nodule is frequently yellowish in colour, and is surrounded by a grey, or bluish or pinkish grey, fibroid ring; outside this again is a pigmented zone, in some cases very distinctly marked.

On section, numbers of these nodules are seen scattered regularly throughout the tissue. Between them is great increase of interstitial tissue, which becomes so extensive in certain cases that the lung feels almost like a cirrhotic liver. On cutting into one of the nodules, which to the touch feel like small beads, it is found to consist of hard fibrous tissue at the periphery, with a gritty centre, the pigmented zone around this varying in size and colour according to the age and occupation of the patient.

Bounded by fibrous bands are numerous large pyriform cavities (bronchiectatic cavities); the apex of each of these cavities usually communicates with a bronchus (of which it appears to be a dilatation), and the base is towards the pleural surface; the walls are hard and thickened, and are lined with a pink, glistening, or translucent membrane, which is continued from the bronchial wall. Radiating from the thickened wall are numerous fibrous bands, some continuous with the deep layer of the pleura, others, more deeply situated, with the peribronchial and perivascular tissue. These fibrous bands are the thickened and fibrous interlobular septa. In them the fibrous nodules, although met with around the bronchi and vessels, are much more numerous and are more prominent. The septa, then, in this case, may be looked upon as the true position of the various changes. (For the nature and mode of formation of bronchiectatic cavities, see § 328.)

Harden a piece of the lung with pleura and a cavity (§ 59), a second (§ 60, 62, or 63), stain (§§ 103 or 104 and 110 (*b*)) and mount (§§ 193 and 199), and mount one section unstained (§ 195).

($\times 50$).—It will be noted at once that there is an enormous increase in the amount of fibrous tissue, more especially along the lines of the interlobular septa, in which also the rounded nodular masses are seen. These latter consist usually of a number of fibrous layers concentrically arranged, the nuclei in which take on the nuclear stain very deeply. In the centre of the mass there is frequently a "core" of yellow, somewhat homogeneous or granular material: the result of

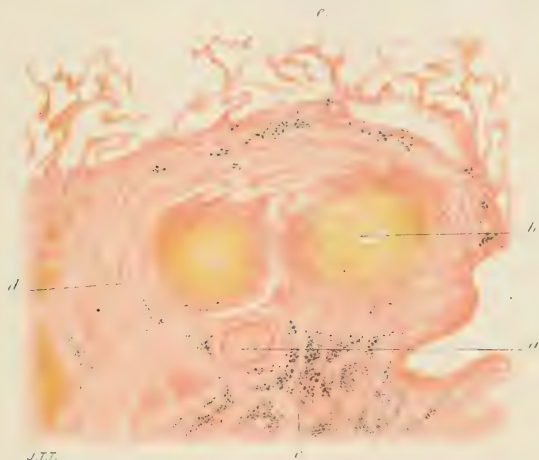


FIG. 142. Section through small fibrous nodule in stone-masons' lung. Stained with picro-carmin. ($\times 50$.)

- a.* Small artery, completely occluded. Endarteritis obliterans.
- b.* Caseous centre.
- c.* Pigment deposited in lymphatics, etc., of young fibrous tissue, marking out position of stone particles.
- d.* Young fibro-cellular tissue, near the margin of the nodule.
- e.* Comparatively healthy lung tissue.

degeneration and breaking down of the cells, which at this point derive little nutriment from the surrounding tissue. Around the yellow centre is a zone of imperfectly vascularised fibrous tissue, whilst still further out is a zone of very vascular and cellular connective tissue. At some points this appears to be little more than a mass of young rounded, deeply stained, connective tissue, cells, in which the greatly distended larger vessels and capillaries stand out very prominently.

The adventitia of the walls of the larger vessels is thickened and cellular, whilst in the intima there is great proliferation of the cells, some of them of considerable size, and many containing granules of carbon pigment. In the walls of the alveoli, the vessels are engorged, and there is some interstitial new formation along the lines of the capillaries. In the air vesicles there is marked evidence of catarrh, and the large epithelial cells contain small granules of black pigment. The air vesicles appear to be smaller, and the epithelium in them, in some cases, is becoming more or less cubical (Fig. 144)—*i.e.* is reverting to the embryonic type. In the peribronchial and perivascular tissue there are similar but less marked changes, pigmentation usually being the most prominent feature. The changes in the bronchi themselves are very similar to those found in coal-miners' lung, but are frequently more acute (§ 315).

($\times 300$).—The fibrous tissue in the septa is almost fully developed, though at certain points, especially near the nodular masses, there appears to be very rapid proliferation of the connective tissue cells. The pink fibrous bands, with the deeply stained elongated nuclei of the fibroblasts, are readily distinguished in the carmine- or fuchsin-stained specimen.

Around the larger vessels the adventitia, in common with the surrounding connective tissue, is undergoing active proliferative changes. The cells are more numerous, and this part of the coat is thickened. In some of the elongated spaces in the thickened adventitia small granules of black pigment and particles of stone may be observed; these silicious particles are usually grey in colour, especially at the margin, but the centre appears to be clear and highly refractile. Pigment is found both in the spaces and in the large cells. In the intima we have the processes seen in connection with obliterative endarteritis (§ 273). In such vessels as have not yet become obliterated the lumen is filled with blood corpuscles. In the rounded fibroid nodules the centre is usually yellow and extremely granular, and is undergoing degenerative changes, as it no longer receives a supply of blood from the obliterated vessels, and there is a condition almost identical with that of the caseating gumma (§ 243). (This caseation is partly the result of an associated tuberculous infection.) Around the yellow mass is well-formed fibrous or cicatricial tissue, to the contraction of which the puckering around the centre of the nodule is due. In the cicatricial tissue few, if any, vessels are visible. In some of the

elongated ovoid spaces in the fibrous tissue the black pigment granules and highly refractile stony particles are seen. These particles are usually unaffected by added hydrochloric acid.

In the zone outside the cicatricial tissue, there is nothing but a mass of connective tissue cells in various stages of development. Some of them are merely rounded nuclei with scarcely a trace of surrounding protoplasm. Others are elongated, and have a delicate periplast, whilst others again are fully formed fibroblasts, with a distinct, often fibrillated, periplast. In some of the cells pigment granules and siliceous particles may be distinguished. Here the vessels are extremely numerous, and are very similar in appearance to those already described in the septa. It is by this zone that the tissue of the nodule is continuous with the tissue of the interlobular and interalveolar septa. The interalveolar septa are somewhat thickened (1) by the distended vessels; (2) by the increase of the interstitial tissue, in the form of small round cells (proliferated connective tissue cells); and (3) by the distended lymph spaces, in which may be found cells containing pigment and stone particles. The epithelium in the air vesicles is undergoing rapid proliferation. Some of the detached cells contain the foreign particles, as do also some of those still *in situ*; others again are undoubtedly free from any of these particles. Some of the epithelial cells are distinctly cubical when the lumen of the air vesicle is, of course, smaller than normal. The changes in the interlobular septa are continued in the peribronchial and perivascular tissue. Bronchitic changes similar to those met with in coal-miners' lung, but usually more acute, are present (§ 325).

The pigment granules are simply those which are met with in every lung, but by their presence they aid us very greatly in localising the siliceous particles.

In *siderosis*, or needle-grinders' lung, changes very similar to those above mentioned, but of a still graver type, are induced.

CHRONIC INTERSTITIAL PNEUMONIA

327. The forms of disease above described are all forms of interstitial pneumonia, but, as already noted, interstitial inflammation may result from acute or lobar, or from catarrhal or lobular, pneumonia. It may also occur in the lungs of children affected with congenital syphilis, though the most common form, which is probably also due to syphilis or to tubercle, is met with in persons in more advanced life.

In the more common form, cirrhosis of the lung (synonyms, "fibroid" phthisis or Corrigan's lung), one lung only may be affected, or the disease may be more advanced in one lung than in the other.

Naked-eye appearances.—On opening the thoracic cavity the affected lung is found to be considerably smaller than the healthy one. It feels firm and fibrous; the visceral pleura is enormously thickened and firmly adherent to the costal layer, though here and there between the two are soft fibrinous masses. On removal, the lung feels almost like a piece of indiarubber, but at some parts, especially towards the base, there may be patches of compensatory emphysema (§ 319). On section, the tissue "cuts" with a firm fibrous feel, and the pleura is found to be enormously thickened, especially in the deeper layer, which is pigmented. In it small tuberculous nodules may usually be seen. In some cases, however, these nodules are absent, especially where the condition is supposed to be of syphilitic origin. Similar nodules may also be found along the lines of the septa and around the bronchi. From the deep layer of the pleura firm fibrous bands pass into the substance of the lung, and run to join the thickened walls of the bronchi and blood vessels. There is often considerable pigmentation of these bands, and also of the peribronchial and perivascular tissue. The vessels and bronchi appear to be crowded together and are dilated. The lining membrane of the dilated bronchus is smooth, pink, and translucent, and is continuous with the mucous membrane of the healthy bronchus.

These dilated bronchi or bronchiectatic cavities are more common here even than in silicosis. They are irregular in shape or somewhat oval, and around the large central cavity we have usually a number of smaller sacs, all communicating with it; these sacs, as a rule, contain a "quantity of pul-taceous material, consisting of inspissated catarrhal secretion" (Hamilton).

The bronchial glands are enlarged and often caseated; other caseous or gummatous-looking masses, about the size of a marble, may often be found in the fibrous bands. These are especially common in the syphilitic form, but they may also occur in the tuberculous variety.

In some cases the interstitial changes appear to be superseded by an acute pneumonic process, which, to some extent, masks to the naked eye the fibroid change, though the interstitial changes are very evident. Prepare as above (§ 326).

To avoid useless repetition, it may be stated at once that here the microscopic changes are very similar to those met with in silicosis.

The thickening of the pleura, the changes in the interlobular septa, and in the peribronchial and perivascular connective tissue; the proliferation of connective tissue along the lines of the lymphatics, along which the irritant material—whether it be stone particles or specific virus—travels; the changes in the vessels—endarteritis obliterans giving rise to the gummatous-like masses in the fibrous tissue, just as in syphilitic disease of the liver (§§ 242 and 243)—and proliferation of the adventitia, are all very similar. The air vesicles are considerably diminished in size, their walls are thickened, and the epithelium is markedly cubical, more so here, indeed, than in silicosis. The fibrous tissue is extremely vascular towards the margins of the septa, and at the periphery of the peribronchial and perivascular tissue, where also it is extremely cellular.

($\times 50$).—The superficial layer of the pleura is little affected, but the deeper layer is thickened and pigmented. The vessels in it are numerous, are distended with blood, and are surrounded by a number of small deeply stained granules (nuclei of young connective tissue cells and leucocytes). The interlobular septa are very vascular, and contain a large number of cells and much fibrous (pink) connective tissue. At the margins of the septa the capillary vessels are numerous, and appear to be those of the thickened interalveolar septa, which are becoming gradually involved in the advancing fibrous mass (§ 325); in this region, too, are evidences both of fibrinous and of catarrhal pneumonic processes. In the wall of a bronchiectatic cavity, there may be recognised some of the elements of the bronchial wall, which have, however, undergone considerable change. There is a formation of new cell elements, by which the proper connective tissue may be gradually displaced, with the result that there is weakening of the wall. The cartilage cells are undergoing either fatty or proliferative changes, the matrix gradually disappears, and there is left simply a mass of small round cells. This is a process similar to that which goes on in the absorption of the connective tissue matrix. Under the low power these cartilage cells appear to be granular, but under the high power their true fatty nature may be distinguished, especially when the section is stained with osmic acid (§ 135). On the lining membrane of the cavity a few columnar cells, with their deeply stained nuclei, can still be distinguished. Running into the weakened cellular wall of the bronchus are the interlobular septa, several of which converge around each bronchial tube.

($\times 300$).—Note the contracted air vesicles, with their thickened and fibrous-looking walls, and their lining of cubical epithelium (the air



FIG. 143.—Section of fibroid lung. Stained with alum haematein and picro-erythrosin. ($\times 40$.)

- a.* Thickened pleura with numerous congested vessels.
- b.* and *g.* Lung tissue collapsed, great increase of fibrous tissue with marked accumulation of pigment.
- c.* Small round-celled infiltration in the wall of a blood vessel.
- d.* Artery with well-marked endarteritis (obliterans).
- e.e.* Sections of bronchi.
- f.* Comparatively normal lung tissue.

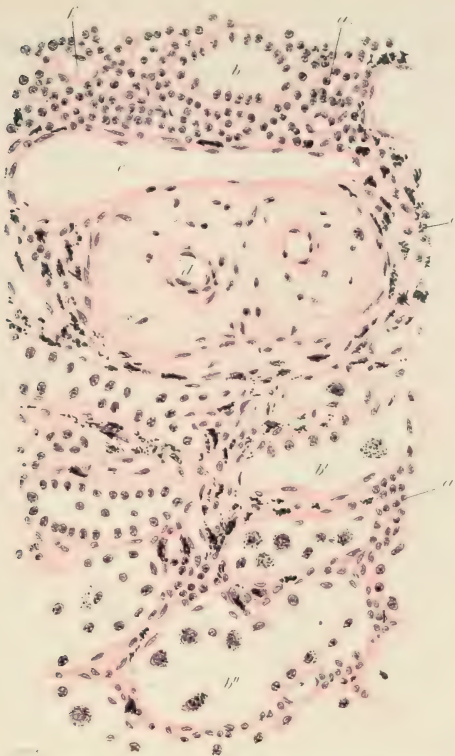


FIG. 144.—Drawing of section of lung: interstitial pneumonia.
Stained with alum hæmatein and picro-erythrosin. ($\times 200$.)

- a.* Mass of fibro-cellular tissue formed in the position of the inter-alveolar septa.
- b.* In this fibrous tissue are small air vesicles, lined with cubical epithelial cells, and containing numerous catarrhal cells, many of which contain pigment.
- b'.* Similar cubical epithelium, near the margin of the mass, where, too, the air vesicles are larger; in *b'* and *b''* the transition of the flattened epithelium to the cubical form is well seen.
- c.* Pigmented connective tissue around the obliterated artery.
- d.* Well-formed arteries with marked endarteritis near the margin of the mass.
- e.* A vein.
- f.* Well-formed blood vessels in the new fibro-cellular tissue.

vesicles outside the fibrous mass are frequently somewhat dilated), the surrounding blood vessels, the changes in the septa and pleura, and lastly, the changes in the wall of the bronchus. Any ordinary case of cirrhotic lung, from syphilis, or any other cause, presents most of these features in such a marked degree that one can have very little doubt as to the nature of the disease, if the examination be carefully made.

BRONCHIECTATIC CAVITIES

328. Bronchiectatic cavities have already been mentioned as occurring in silicosis, and in the various forms of chronic interstitial pneumonia. They are also found in almost all forms of chronic phthisis, in which interstitial inflammatory changes are set up.

Naked-eye appearances.—These cavities are usually of moderate size, and are frequently sacculated or globular in form, especially when they are due to the weakening of the bronchial wall by inflammatory changes, such as have been described in the two previous sections.

Angular cavities are caused by traction exerted on the walls of the bronchi by the contracting fibrous bands—the cirrhotic interlobular

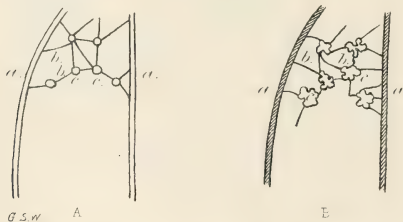


FIG. 145. Diagram to represent the method of formation of bronchiectatic cavities by the traction of the cicatricial tissue in the interlobular septa on the weakened bronchial walls.

septa—a process which may be best explained by means of a diagram.

The lines *aa* represent the walls of the chest to which the pleura is closely apposed, naturally, because the cavities are air-tight, but also as the result of inflammatory thickenings and adhesions. The lines *bb* are supposed to represent the interlobular septa, running first from one side of the chest to the wall of a bronchus, *c*; then on to another

bronchus, and lastly, to the opposite chest wall. As these fibrous bands contract, there is traction on the walls of the bronchi, and also on the walls of the chest; and as the latter are much the more rigid, the former have to give way at a point where the septa run into their walls. At the same time the chest wall becomes slightly flattened, especially at the upper part, but this is not nearly so noticeable as is the change in shape, and increase in size, of the bronchial tube. In the cavity the lining membrane is smooth, glistening, and translucent, and has a pink tinge, owing to its extreme vascularity.

Another form of bronchiectatic cavity is caused by the accumulation of catarrhal products in the bronchus. This leads first to distension, and then to the formation of a cavity of moderate size, as inflammatory processes are set up in the walls by the irritant accumulated material. Such cavities are usually met with in considerable numbers; they are more or less fusiform or spindle-shaped, and may have the same pink, glistening, lining membrane as the above form, or they may be lined by a soft caseous material, especially in tuberculous cases.

Still another form is that met with in ulcerative bronchiectasis following catarrhal pneumonia. In this there is ulceration of the bronchus and a giving way and distension at the weakened point.

Whilst on the subject of cavities, or vomicæ, the form in which there is extensive softening of the lung tissue, as a result of various inflammatory and caseous processes, may be mentioned. A large cavity is formed, and into this one or several bronchi open; by these the softened contents of the cavity are carried away. Such a cavity may usually be recognised by its greater size, the more or less irregular outline, the "several openings of the bronchi into it, and by the bands of more resistant fibrous tissue which run from side to side of the cavity" (Hamilton). These are not blood vessels, as generally supposed, but are bands of fibrous tissue or thickened interlobular septa,—very frequently, however, containing branches of blood vessels embedded in their substance. Small aneurisms have been described as occurring in some of these vessels. It is now held by most authorities that these large irregular cavities are the result of the running together of several smaller cavities, many of which are formed during the course of rapid phthisis. When a cavity is once formed it goes on enlarging, the surrounding fibrous tissue is comparatively non-resistant, and repeated coughing brings about a rapid distension. The pleura over such a cavity is almost invariably much thickened.

BROWN INDURATION OF THE LUNG

329. Synonyms, "Brown Œdema," "Chronic Venous Congestion" of the lung. This condition is most frequently associated with disease of the valves of the heart, especially of the mitral valve, though it often occurs in connection with aortic disease.

Naked-eye appearances.—The lung is usually somewhat more voluminous than normal. The pleura has a peculiar reddish-purple colour, through which the deeply pigmented interlobular septa stand out very prominently. At the free borders of the lung there is frequently some emphysema; here also are firm, more deeply coloured, wedge shaped patches of a deep plum colour, sometimes with a tinge of brown, which project above, and are sharply defined from, the surrounding tissue. These patches are solid and sink in water; they constitute the so-called pulmonary apoplexies. On section, in place of the bright arterial red colour of acute congestion, there is a peculiar brownish or brick-red colour, and, on pressure, there exudes brownish-red serum, mixed with air; there is œdema, and at certain points, marked emphysema. Scattered over the section, especially at the posterior and lower part of the lung, and not sharply marked off from the surrounding tissue, are firm patches, varying in diameter from half an inch to an inch. They are not solid, but are much firmer and harsher than the surrounding tissue; when cut into they have a peculiar gritty feel, and from them reddish-brown serum, mixed with air, may be squeezed. Examine this exudation ($\times 300$). It consists (1) of granules of golden-brown pigment; (2) of large flattened cells, in which are numerous similar granules; and (3) of red blood corpuscles in various stages of disintegration.

The interlobular septa, the deep layer of the pleura, and the bronchial glands, are deeply pigmented, and stand out very prominently, and the latter are also often enlarged and indurated. On the surface the dilated branches of the pulmonary vessels stand out more prominently, and therefore appear to be more numerous than in the normal condition. (See § 309.)

The mucous membrane of a bronchus is usually deeply congested, folded, and corrugated, and has a characteristic watery or œdematous appearance.

Harden three pieces, one in which the œdema is marked, a second piece of one of the brown patches, and a third with a wedge-shaped

pulmonary apoplexy or hæmorrhage, some of the pleura, and a small bronchus (§ 62), and mount unstained (§ 195).

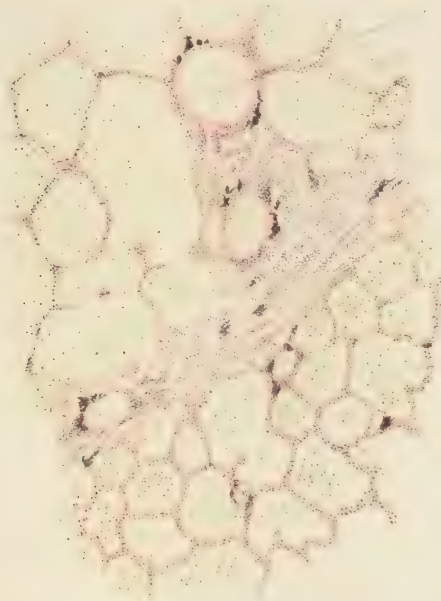


FIG. 146.—Section of piece of lung in which there is well-marked chronic venous congestion and a hæmorrhagic infarction. Stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

- a.* A blood vessel.
- b.* Air vesicle filled with red blood corpuscles; the nuclei of a few leucocytes and epithelial cells are seen.
- c.* Thickened and cellular interlobular septum.
- d.* Thickened interalveolar septum—thickening due to varicose and distended condition of the capillaries.
- e.* Air vesicles in which are numerous pigmented catarrhal cells and red blood corpuscles, from which pigment is ultimately derived.

Above the fibro-cellular band is the infarcted area, below it an area in which chronic venous congestion or brown induration is marked.

Harden one piece of œdematous lung by heat (§ 73), stain (§ 105), and mount (§§ 193 and 199).

($\times 50$).—The pleura is greatly thickened, especially the deeper layer, which is also deeply pigmented. The pigment is black and golden-brown. The interlobular septa, the perivascular and peribronchial tissues, are also thickened and pigmented. In the solid wedge-shaped mass the air vesicles also have their walls thickened and pigmented, but this is partially masked by the enormous number of red blood corpuscles which have escaped. On the pleural surface

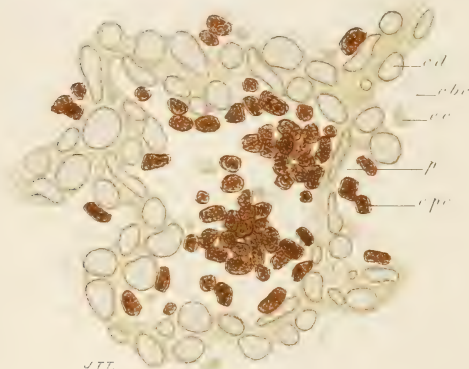


FIG. 147.—Drawing from section of brown induration of the lung.
Unstained. ($\times 300$.)

- c.d.* Distended capillaries of interalveolar septa.
- c.b.c.* Coloured blood corpuscles lying free in the air vesicle.
- e.c.* Epithelial cell, detached.
- e.p.c.* Epithelial or catarrhal cell, containing a large quantity of altered blood pigment.
- p.* Pigment in lymphatics of interalveolar septum.

At the point from which this was taken the pigmentation was very marked; the varicosity of the vessels is here well seen.

there may be slight inflammatory changes, but these are by no means constant.

In the portions in which brown induration is well marked, the changes are very characteristic. The walls of the air vesicles are thickened and pigmented, and have a peculiar beaded or varicose appearance; in the beads (or loops) there is a greenish granular material—coloured blood corpuscles. Within the air vesicles similar corpuscles may be observed, and also a number of large flattened cells,

many of which contain pigment. Most of these cells are lying free in the alveolar cavity, but others are attached to the beaded-looking wall; the interlobular septa are thickened.

In the walls of the bronchus the small blood vessels are enormously distended. There is, throughout, an increase of fibrous tissue, which, in a stained specimen, is very prominent. The mucous membrane is thrown into folds, and the tortuous blood vessels, which come very near the surface, may, even in a small bronchus, rupture into the lumen. As a rule, little of the bronchial epithelium is left; it is detached by the serum exuded from the distended blood vessels almost as rapidly as it is formed.

($\times 300$).—First examine the air vesicles, in which are numerous flattened cells lying free, or closely applied to the wall; the former, comparatively few in number, may be seen in section as nucleated spindle-shaped cells. Most of them contain granules of golden-brown pigment, which stand out very prominently. Along with the large detached cells are a few coloured blood corpuscles. Lying beneath the attached epithelial cells are the capillary vessels of the wall; they are much distended and varicose, and appear as loops or sections of vessels projecting into the air cavity. They were long mistaken for epithelial cells, but by the aid of picro-carmin or alum hæmatein and van Gieson's stain, the coloured blood corpuscles may be demonstrated in the lumen of the pink-walled vessel. These vessels have a double outline, and in some cases there appears to be great thickening of their walls, a condition similar to that described in nutmeg liver (§ 238). In the wall of the vesicle—that is, along the course of the lymphatics—pigment, much deeper in colour than that in the cells, but still golden-brown, is deposited. A small proportion of black pigment, carbon pigment derived from without, is also seen in these positions, but the bulk of the pigment is derived from altered red blood corpuscles; it lies in the lymph spaces, free or enclosed, either in epithelial cells from the air vesicles, or in endothelial or connective tissue cells.

There are similar pigments in the interlobular septa and in the deep layer of the pleura, to both of which they have been carried from the air vesicles by the lymphatics; also in the peribronchial and perivascular lymphatics. In all these situations there is an increase of fibro-cellular tissue, which is well seen in the stained specimen; after the pigmentation, the enormous distension of the vessels is the most marked feature, and it is to this dilatation, especially, that the

thickening of the pleura and the increase in volume of the lung are due.

In the walls of the smaller bronchi note the great congestion of the mucous membrane. The vessels here, as in the walls of the alveoli, are distended, lengthened, and varicose, and their walls thickened. At certain points they are so much dilated that they form a cavernous structure, almost like that seen in the centre of a lobule in advanced nutmeg liver. The muscular coat is usually somewhat atrophied, owing, apparently, to distension of the vessel and consequent pressure on the muscle. The basement membrane is swollen and œdematous, and the few cells covering it are flattened, cubical, or irregularly columnar. The most marked vascular changes take place around the bronchi and beneath the pleura, towards the base of the lung, but they are by no means confined to these situations. In the naked-eye examination it was observed that there was dilatation and prominence of the vessels of the lung. This is evidently due, partly, to distension, but also, partly, to hyaline or fibroid thickening of the tunica intima, which in this condition, as in the granular contracted kidney, is fairly well marked.

The solid wedge-shaped, plum-coloured or brick-red patches,—pulmonary apoplexies, as they are called,—frequently coincide with the distribution of the bronchus; the bronchus, as well as the terminal air cavities, in such cases being filled with blood. Otherwise they have all the appearances presented by the remainder of the lung. It must be remembered, however, that the hæmorrhages are usually met with only where the brown induration is due to valvular disease of the heart, especially of the mitral valve.

($\times 50$).—A clot of some standing may be traced into the branch of the pulmonary artery supplying the infarcted area in which the alveoli are considerably enlarged and distended with a coagulum consisting largely of red blood corpuscles (see Fig. 146). The central bronchus, though often filled with red corpuscles, may be quite free from coagulum of any kind. At the margin of the infarcted area there is usually some evidence of inflammatory reaction—cell infiltration—some slight collapse of a few of the air vesicles, and great increase in the number of young cells running along the line of the larger septa. The tissue around the infarcted area presents the typical appearances associated with chronic venous congestion.

($\times 300$).—Verify the above description.

Brown induration of the lung is simply a secondary condition induced by a primary disease of the heart. It first appears as a chronic venous congestion, in which there is an accompanying exudation of serum from the capillaries: this causes separation of a considerable part of the epithelium in both air vesicles and bronchi. At the



FIG. 148.—(Edema of lung following chronic venous congestion. Stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

- a.* Alveolar space containing coagulated albumin and a few nuclei of leucocytes and epithelial cells.
- b.* Alveolar space in which are a number of red blood corpuscles.
- c.* Thickened interalveolar septum.
- d.* Pigmented interalveolar septum.
- e.* Thickened adventitia with deeply pigmented perivascular lymphatics.
- f.* Coagulated fibrin near the centre of the coagulum in an alveolus or air vesicle.

same time blood corpuscles escape into the alveoli, and are taken up by the altered epithelium; these are taken into the lymphatic system of the interalveolar septa, from which the pigment is distributed to all the positions above mentioned, including the bronchial glands. The vessels become more distended, more tortuous and thickened, and so the condition of brown induration is gradually developed. A

small portion of the pigment is carbon pigment; but by treating a section with a solution of ferrocyanide of potassium, and then with a dilute solution of hydrochloric acid, a blue reaction is obtained, even with some of the perfectly black pigment, which indicates that it contains iron and is probably derived from the blood.

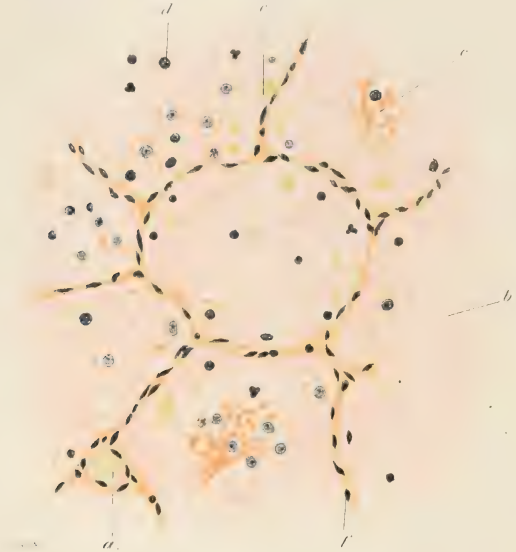


FIG. 149.—Section of edematous lung. Stained with alum haematein and van Gieson's stain. ($\times 350$.)

- a.* Distended blood vessel.
- b.* Granular-looking coagulated albumin.
- c.* Fibrin in centre of coagulum.
- d.* Proliferated or separated epithelial cell.
- e.* Extravasated red blood corpuscles, some of which may be taken up by epithelial cells.
- f.* Somewhat prominent interalveolar septum.

Between this brown induration and rapid venous congestion are many intermediate stages. The rapid venous congestion is characterised by the water-logged condition of the lung, the lymphatics being unable to carry off all the fluid as it is exuded. On section there is usually marked congestion, whilst from the cut surface there

exudes an enormous quantity of frothy, watery fluid. The air vesicles soon become filled with fluid.

($\times 50$).—The alveoli are filled with a hyaline, brownish or pinkish material, evidently coagulated albumin. In this are embedded a few polymorpho-nuclear leucocytes and a number of larger mononucleated cells, derived from the epithelium covering the walls of the alveoli. The peribronchial and perivascular lymphatics contain much brownish or black pigment—altered hæmoglobin of the red blood corpuscles. In acute œdema this pigmentation is not observed, but in the œdema of chronic venous congestion it is always a well-marked feature. Pigmentation of the interalveolar septa may also be seen, this in some cases accounting for the prominence of the alveolar walls.

($\times 300$).—The coagulum, now seen to be slightly granular, fills the alveoli; the congested vessels stand out prominently, and the walls of the alveoli are outlined by these and by the endothelium of the blood vessels and the epithelium lining the air vessels. Leucocytes and mononuclear cells, large and small, are present in small numbers only. A few red blood corpuscles are also to be seen; these have escaped from the distended blood vessels, and are ingested by the epithelial cells, which elaborate from them the brown pigment that is seen in the interalveolar septa, the lymphatics of the perivascular and peribronchial tissue, the deep layer of the pleura, the glands at the root of the lung, etc.

FAT EMBOLISM OF THE LUNG

330. There are few naked-eye changes in the lung in this condition beyond some œdema and congestion, which are specially marked where the embolism follows diabetic coma or fracture of a bone, especially of one of the cranial bones. The following case was diagnosed during life as one of fat embolism, due to fracture of one of the cranial bones. There was intense congestion of both lungs, accompanied by a number of bright subpleural hæmorrhages which, though small, were very distinctly seen. On examination of a fresh section (§ 36), $\times 50$, bright refractile globules were observed in a number of the capillary vessels, and also in some of the larger branches of the pulmonary artery. These were stained black with osmic acid. In the stained specimen some of the emboli in the larger vessels were distinctly seen as elongated masses, completely filling the vessel, and

ending at its point of bifurcation. At the proximal end of some of the fat emboli the vessel had ruptured, and there was an extravasation of blood into the surrounding air vesicles; most of the emboli and

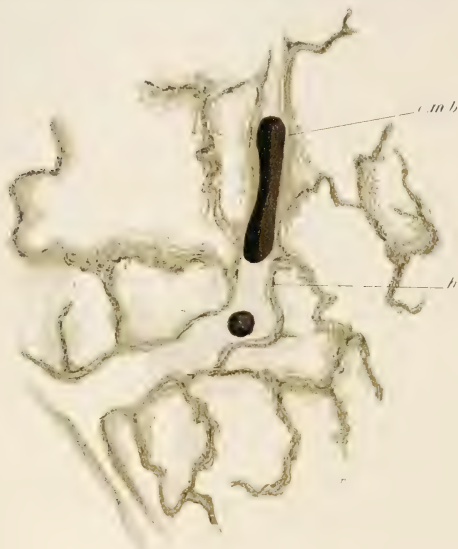


FIG. 150. —Fat embolism of the lung. Stained with osmic acid.
($\times 100$.)

emb. Fat embolus stained black, filling one of the larger vessels.

h. Mass of coloured blood corpuscles in an air vesicle, the result of rupture of some of the smaller blood vessels behind the embolus.

hæmorrhages were situated near the surface, where the terminal branches of the blood vessels are usually distributed.

Harden (§ 60 or 63), stain (§ 135), and mount (§ 195).

($\times 50$ and $\times 300$).—Confirm the above points, and observe the different sizes and positions of the fatty globules stained black by osmic acid. Some are extremely small, and are in the centre of the blood mass. Others, larger and crescentic, are adherent to the wall of the vessel; whilst others again completely fill the lumina of vessels of very various diameters.

Similar small hæmorrhages are met with in cases of phosphorus poisoning, in septic fevers, anthrax, etc., and frequently even in cases of active hyperæmia.

TUBERCULOSIS

331. Phthisis and tuberculosis are intimately associated, and must be described together. Tuberculosis may be defined as an infective disease brought about by the activity of a specific bacillus, which is enabled to live within the body, where, by its presence, it sets up irritative and proliferative changes in either epithelial, endothelial, or connective tissues, such changes being followed by fibroid or caseous changes, according (*a*) to the number and activity of the bacilli attacking; and (*b*) to the state of nutrition and powers of resistance of the tissues attacked.

PHTHISIS

332. Pulmonary phthisis results from these irritative inflammatory and degenerative changes, and may be defined as a disease of the lung, characterised first by consolidation, the result of the formation of tubercle of different kinds, accompanied by the various forms of pneumonia—interstitial, croupous, and catarrhal—with obliteration of the blood vessels and disturbance of the lymphatic circulation, fibrous tissue formation, or caseation and ulceration, as the case may be. Changes in the walls of the bronchi lead to weakening, or even to ulceration; those in the septa may lead to fibrous tissue formation, whilst similar changes or caseation may result throughout the whole of the lung substance. Caseation and cavity formation are most frequent in the upper part of the lung, near the apex, where, too, the process is, as a rule, more chronic, but more advanced.

TUBERCLE BACILLI

333. The association of the tubercle bacillus with tuberculous disease cannot now be doubted; it is found in the lungs and sputum in various forms of tuberculosis and phthisis; it has also been demonstrated in tuberculosis of the intestine; around the vessels in tuberculous inflammation of the membranes of the brain; in tubercle of the liver, and of other organs of the body; and in tuberculous eruptions of the skin. It may be well at this point to examine the

tubercle bacillus, in order that it may be recognised in the various specimens of tuberculosis and phthisis that are examined.

Prepare a specimen of sputum (§§ 171 and 182) and stain (§ 183). When thus prepared, tubercle bacilli may be seen ($\times 1000$) as delicate

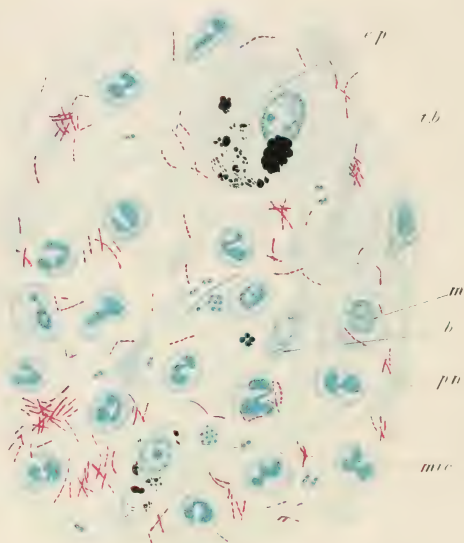


FIG. 151.—Sputum from a case of phthisis. Stained by the Ziehl-Neelsen method, with methylene-blue counterstain. ($\times 1000$.)

t.b. Tubercle bacilli. Stained by basic fuchsin. Note arrangement and plain and beaded appearance.

cp. Epithelial cell containing vacuoles and masses of carbon pigment.

m. Mononuclear cell containing ingested tubercle bacilli.

pn. Polymorpho-nuclear cells, one apparently containing ingested tubercle bacilli.

b. Bacilli (not tubercle bacilli), stained by contrast stain.

mic. Micrococci, stained by contrast stain.

rods or threads, 1.3 to 3.5μ in length, and about 0.3μ in thickness, though they may appear to be somewhat thicker. Speaking roughly, the length is equal to from one-quarter to one-half the diameter of a red blood corpuscle. The bacilli are usually slightly curved, or two

are arranged end to end, so as to contain an angle. At first sight they appear to be homogeneous; but, on more careful examination, under this very high power, from two to six pseudo-spores or small ovoid or rounded clear spaces may be seen at intervals in the stained thread; in some cases these are so prominent that they appear to project beyond the straight outline of the bacillus, an appearance that has led to the thread being sometimes described as a chain of cocci,—a coccotrix. The bacilli are quite motionless. Sometimes they may be imperfectly stained or the protoplasm may appear granular, and almost as a little rod of *débris*; usually they are lying free near the epithelial and pus cells, but in some cases they are actually embedded in the protoplasmic substance of these cells, especially of those with the lobulated nuclei. They appear to exert an influence on the tissues even at a distance, and where they are present in considerable numbers there will usually be found in the immediate neighbourhood a small portion of tissue that has undergone marked degenerative changes, evidenced by the fact that the cells are now imperfectly stained by carmine or the anilin dyes. After a time these cells lose their outlines; they become more and more indistinct, and eventually nothing but a shadow of the cell is left, this occurring where the caseous degeneration is advanced. Even outside the zone in which the bacilli are numerous the cells become hyaline and take on stains imperfectly, although the bacilli have not yet advanced into this area; on the other hand, in the zone in which they are found, some semblance of form is still seen in the tissue cells, and many are comparatively normal; in the zone that they have left, caseation is well marked, and there is little evidence of the nature of the tissue from which the caseous material is derived. These points should always be borne in mind when any examination of tuberculous tissue is made.

·DISSEMINATED MILIARY TUBERCULOSIS

334. *Disseminated miliary tuberculosis* is met with in acute general tuberculosis, especially in children and in young adults.

Naked-eye appearances.—The lung is usually deeply congested; scattered over the congested surface are numerous pale, pearly, translucent or gelatinous-looking nodules about the size of small shot, which stand out very distinctly from the surrounding tissue; there is usually little or no pleurisy. At first sight the nodules appear

to be scattered indiscriminately over the surface of the lung; but on more careful examination it will be found that they are situated in the lines of the interlobular septa, especially at their points of junction. A fresh section, like the surface, is deeply congested and



FIG. 152.—Advanced miliary tuberculosis of the lung. Stained with alum hæmatein and van Gieson's stain. ($\times 90$.)

- a.* Caseating tuberculous focus, with
- b.* A few leucocytes at the periphery.
- c.* Congested alveolar capillary.
- d.* Well-marked catarrhal pneumonia surrounding the central caseous tubercle.

Note that the blood vessels are occluded in the tubercle nodule in the centre of the mass.

of a bright scarlet colour; the nodules are usually more numerous in one lung than in the other, and affect one lobe more than the other. They are found in the deeper layer of the pleura at the points where the septa run into it, and also along the lines of the larger septa, though some are in the lobule itself. A few of these may be

grouped together, but this is comparatively rare. Harden (§ 58, 62, or 63) and stain (§§ 102 or 104 and 183 *et seq.*).

($\times 50$).—Note that the tuberculous masses are growing in the interlobular septa, or in some cases from an interalveolar septum, and that each is composed of one or more follicles. In all essential points they resemble the tuberculous masses in the liver (§ 246); but giant cells, containing a large number of nuclei, are comparatively rarely seen, and usually in place of them is a granular yellow caseous mass. Around it is an open reticular tissue, the meshes of which are somewhat elongated, and are concentrically arranged. In the elongated spaces are few small round cells, but there are numerous endothelioid cells, somewhat irregular in shape, many of them containing two or more nuclei. At the periphery of the tubercle nodule, numerous small round cells are found, which appear to be arranged in rows, these rows enclosing spaces. The spaces appear to be somewhat contracted alveoli, of which the rows of round cells form the thickened walls. Projecting into the air vesicle from the thickened wall are similar masses of endothelioid cells, pushing before them the epithelial layer. In the immediate neighbourhood of the solid area the thickening of the alveolar walls is proceeding, the cavities are smaller and appear collapsed.

Examine an artery and a bronchus, and notice that in some cases slight round cell infiltration is the only evidence of tuberculous affection. In the immediate neighbourhood of the tubercle nodule marked proliferation of the epithelium lining the air cavities may be noted.

($\times 300$).—The caseous centre is easily made out. Around it are numerous endothelial cells; these are very irregular in shape and size, some containing but one nucleus, whilst others have as many as four. The reticulum is not very readily distinguished under this power, but the leucocytes and small mononuclear cells, along with the larger cells, are well seen. Towards the periphery of the mass the appearances are very distinctive. Collapsed air vesicles are bounded by the greatly thickened alveolar walls, in which there is evidently active proliferation of the connective tissue cells. The masses of large endothelioid cells, however, are seen pushing their way into the cavity, forcing before them the epithelial lining. The cells of which this lining is composed are in a condition very similar to that met with in interstitial pneumonia, but they are hyaline or granular and swollen. They are cubical, and in some cases are of very great size

(§ 327). In the immediate neighbourhood of the tubercle nodule the interalveolar septa are considerably thickened, and epithelial changes are beginning; the air vesicles are collapsed, and there is no marked catarrhal or croupous inflammatory exudation, but outside this zone there may be distinct catarrhal changes. The caseation in the centre of the tubercle mass is similar to that met with in caseation

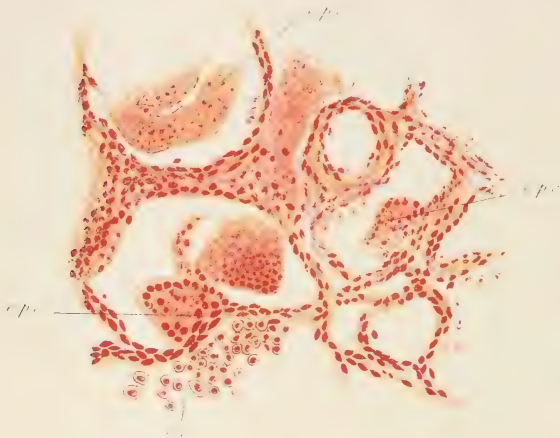


FIG. 153.—Section of lung. Acute miliary tuberculosis. Stained with picro-carmin. ($\times 300$.)

e.c. Growth of large endothelioid cells.

ep.c. Growth of epithelial cells into alveolus. These cells are arranged somewhat in columns, and are undergoing rapid caseation. The mass is yellow and homogeneous at its surface.

Between the air vesicles the septa are somewhat thickened, and some of the air vesicles are apparently diminished in size by the encroaching epithelium.

of a gumma. The tuberculous masses are purely extravascular, as may be proved by injecting such a lung; and as fresh tubercle follicles are formed around the primary one, that in the centre is cut off from its nutritive supply, and undergoes caseous degeneration. In most cases this caseation comes on before the formation of the giant cell, immediately after the abnormal growth of the large endothelioid cells has taken place; this is especially the case where the disease is very

acute, when there may be a condition almost like that to be described as broncho-pneumonic phthisis (§§ 335 and 336). In the specially stained specimen now look for the tubercle bacilli, which may be seen as red rods lying in the lymph spaces. Some of them may be in the giant cell, but they are best seen as they lie in the meshes of the network surrounding the giant cell, but sometimes, also, in the proliferating epithelium. (For appearance of these bacilli, see Fig. 151.)

The larger masses of tubercle will be best described under chronic phthisis (§ 337), in the production of which they play a very prominent part.

CASEOUS BRONCHO-PNEUMONIC TUBERCLE

335. Caseous broncho-pneumonic tubercle is met with in children as what appears to be a form of acute tuberculosis, specially confined to the lung, or, at any rate, more advanced in this position than in any other organ in the body.

Naked-eye appearances.—The lung is congested and sometimes slightly œdematous, with here and there patches of collapse. Standing out prominently from the congested surface, either through the pleura or from the cut section, are a number of small nodules, one-twelfth to one-sixth of an inch (2-5 mm.) in diameter. They are most numerous at the apices and towards the roots of the lung, and may be rounded or irregular in outline, some of them appearing to be branched and elongated. Each has a typical appearance; at the periphery the tissue is firm, greyish, and gelatinous, whilst the centre is softer, pale yellow, and granular.

On squeezing the section a quantity of tenacious, muco-purulent material is pressed from the bronchi, especially the smaller ones (§§ 315 and 316).

Harden (§§ 58 and 62 or 63) and stain (§ 183 *et seq.*).

($\times 50$ or $\times 20$).—All the patches of the solidified tissue have a similar arrangement, the details differing only according to the direction in which the section is made through a bronchus, with its dependent air vesicles. In a transverse section of a terminal bronchiole, note the following features:—Towards the centre, or a little to one side of the solid area, is a rounded opening, or what was an opening, containing a plug of small rounded granules—catarrhal or purulent-looking cells. In the centre is a quantity of more or less homogeneous material, which stains yellow with picro-carminic (§ 102)

and with alum hæmatein and van Gieson's stain (§ 103); in this yellow material the outlines of the individual air vesicles can usually scarcely

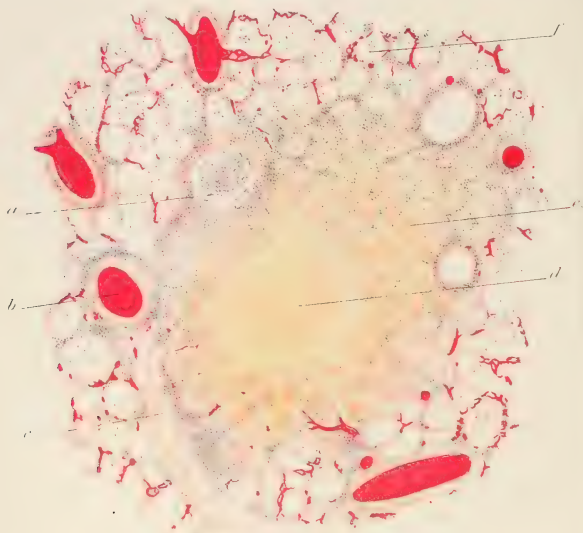


FIG. 154.—Section of a lung affected with tuberculous broncho-pneumonia injected with gelatin carmine. Stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

- a. Bronchus containing catarrhal exudation.
- b. Branch of pulmonary artery containing gelatin injection mass.
- c. An interlobular septum.
- d. Central caseous mass of the tuberculous broncho-pneumonic patch.
- e. Coagulative necroses seen in broncho-pneumonic patches around central caseous area.
- f. Early catarrhal pneumonia.

Note that the central part of the tubercle is now entirely avascular. The infection seldom passes into the area of coagulative necrosis.

be discerned. Around the caseous centre is a zone of air vesicles in which there is no caseation, but in which are evidences of catarrhal (§ 321) or acute fibrinous (§§ 312 and 313) pneumonic deposits; the

interalveolar septa are thickened, and stand out somewhat prominently. Around the bronchi there is also an amount of thickening of the adventitia, due apparently to peribronchitis, similar to that met with



FIG. 155.—Section of lung in which there is caseous broncho-pneumonia. Stained by Weigert's elastic tissue stain and alum carmine. ($\times 90$.)

- a.* Outline of nearly normal alveolar wall.
- b.* Consolidated broncho-pneumonic area in which the elastic tissue of the interalveolar septa is well seen.
- c.* Caseated broncho-pneumonic patch in which the elastic fibres still persist and are deeply stained.
- d.* Elastic fibre of the wall of a large artery.
- e.* Proliferating intima, the result of extension of the tuberculous process from the outside of the vessel, through the elastic tissue, the fibrils of which are widely separated by the new but now caseating tissue.

in catarrhal pneumonia (§ 321). Fully developed giant cell tubercle is comparatively rare, caseation taking place before the organisation of the follicle has reached this stage. The changes can best be

observed where the process is beginning, or just at the margins of the caseating area seen in a "Weigert"-stained specimen (§ 167).

($\times 90$).—Examine some of the consolidated patches, in which between the elastic tissue brought out by the Weigert's stain, much new tissue has been formed. The tubercular process whilst bringing about separation of the elastic fibres, does not cause their degeneration. The alveolar walls may be seen distinctly outlined by the elastic tissue which persists even in a caseous mass. The lines of the blood vessels may also be seen similarly marked out; whilst the invasion of the walls of the larger vessels by the tubercle bacilli and the changes induced by the presence of these organisms may be readily followed. The extension of the process from the adventitia of certain of the vessels through the muscular coat to the intima is clearly demonstrable.

($\times 300$).—Examine a small bronchus or an alveolar passage, and note that it is filled with cells which closely resemble the catarrhal cells—seen under the low power as granules. Amongst these in the specimen stained by the Ziehl-Neelsen method (§ 183) are numerous rod shaped tubercle bacilli. In the centre of the acinus, where the caseation is most advanced, a mass of granular debris, stained yellow, may be observed. Near the margin, tubercle bacilli are found in the interalveolar septa, and in some cases are exceedingly numerous. At the margin of the caseating mass the epithelial cells are undergoing changes other than simple catarrh; they appear to be arranged in columnar processes—(this is especially well seen in a fresh section stained in picro-carmin)—extending into the alveolus for some little distance. The cells of which these columns are composed have a peculiar hyaline appearance, and they very rapidly become caseous; they are stained yellow with picric acid. In the true catarrhal cells there is frequently an œdematous condition or a simple fatty degeneration—changes quite distinct from the caseous condition.

Examine the fibrous septa near the caseous centre, and note that in them and in the interalveolar septa there is a great amount of small cell infiltration; nutrition is cut off by the occlusion of the vessels, and this assists the caseous metamorphosis. In very thin sections tubercle bacilli may be distinguished, not only in the lymph spaces in the thickened interalveolar septa, but also in the epithelial cells which line the air vesicles at the point where the proliferation is taking place. Confirm the appearances in the Weigert-stained specimen in which the tuberculous character of the process is evident.

The catarrhal pneumonic cells, the proliferation of the cells of the intima of the vessels and of the interalveolar septa, and the persistence of the elastic tissue in the caseating proliferating tissue, may all be readily made out.

It should be noted that the air cavities in connection with the terminal bronchioles are the areas in which these changes are observed ; and if a vertical section be made through the bronchiole with its terminal cavities, the caseous mass is always situated near the bronchiole, and the pneumonic zone nearer the periphery.

ACUTE PHTHISIS

336. Acute, rapid phthisis is a condition in which there appears to be a process almost like broncho-pneumonic tubercle, associated, however, with more extensive changes.

Naked-eye appearances.—The pleura is, as a rule, somewhat thickened, especially over the apex. The tissue of the lung is solid, and beneath the pleura large pale yellow patches are seen, radiating from which are numerous similar solid bands. On section, there is usually evidence of a more chronic process at the apex. There may be a cavity of considerable size, the walls of which are firm, indurated, and pigmented ; over it the pleura is thickened. Around the cavity the changes are more acute, but the appearances are evidently considerably modified by the presence of the more chronic changes. In the lower part of the lung, however, the acute changes are more prominent and characteristic.

Scattered over its surface are large, rounded, pale yellow patches, from which processes run out in the same manner as under the pleura. Between the yellow patches—which in shape may be compared to bunches of grapes, of which the bronchioles form the “stalks”—are bright red lines, in which the caseous process has not as yet become marked. Towards the base the yellow patches are so large and so numerous that they run together, and obscure every other change.

On pressure there exudes from the bronchi a thick, tenacious, muco-purulent material, the walls of the bronchi are thickened and somewhat gelatinous looking ; the bronchial glands may be swollen and oedematous, or softened and caseous.

The yellow patches, and even a great part of the lung, may

present appearances similar to those met with in broncho-pneumonic tuberculosis, except that the destructive processes are more pronounced; there may be patches of grey granulations, wedge-shaped near the pleural surface, racemose, or in clumps in the substance of the lung, all of which are surrounded by pneumonic patches, are in various stages of caseation, and are more chronic than the form first described; the microscopic changes vary considerably.

Harden pieces of the different parts of the lung (§ 56, 59, 62, or 63), stain (§§ 102 or 103 and 183 *et seq.*), and mount (§§ 195 or 193 and 199).

($\times 50$).—Examine one of the pale yellow patches, and note that it is made up of a series of areas, each of which has a caseous centre, in which are involved the walls of the alveoli as well as their contents. At this point there are no vessels. Further from the centre is a zone, in which the alveolar walls are somewhat thickened, and where the blood vessels are not very readily seen. There is considerable catarrh in this position; parts of the catarrhal products are stained black in a section treated with osmic acid. Still further from the centre are early catarrhal or acute croupous pneumonic patches—readily recognised—and in this region the capillary vessels are usually considerably distended. These areas have frequently become fused by the extension of the pneumonic process; in such cases great destruction of tissue occurs. The pleura is thickened and extremely vascular, with a considerable number of granulation loops passing to the surface, and at points the two pleural surfaces have become adherent. In tissue taken from near the apex there are usually evidences of the presence of a chronic interstitial pneumonia, with chronic tubercle, to be afterwards described; whilst around the parts thus affected the tissues may be in an advanced state of caseation, smaller cavities being formed by the breaking down and evacuation of the caseous material. The vessels around these patches, as in interstitial pneumonia (§ 327), are in an advanced stage of endarteritis obliterans (§ 273).

Around the bronchi are changes similar to those met with in broncho-pneumonia; tubercle nodules in an early stage of development may sometimes be met with in this position.

($\times 300$).—Confirm the above appearances. The course of the disease is apparently very rapid, but the rapidity varies in different cases. If the patches are more or less separated, and the caseous changes are taking place only at intervals, the course of the disease

is comparatively slow, and the appearances, both naked-eye and microscopic, closely resemble those found in broncho-pneumonic tubercle; but when the masses run together rapidly, owing to the rapidity of the catarrhal and croupous pneumonic changes, and there is formation of cavities of considerable size, the disease usually runs an extremely acute course. In whichever form the disease is met with, tubercle bacilli are found in large numbers, especially at the points where the proliferation of epithelial cells is greatest, and also where the connective tissue cells are undergoing rapid proliferation. Where the caseation is advanced, the bacilli are not so readily distinguished. To find them, it is necessary to use a somewhat higher power ($\times 600$) than that used in the examination of sputum.

COMMON CHRONIC PHTHISIS

337. This form of lung disease runs a very slow course, the symptoms during life being very well marked, and the pathological changes extremely characteristic.

Naked-eye appearances.—On opening the chest it will be noted that the lungs are firmly adherent to the surrounding tissues, especially at their apices (if the disease occurs on both sides); frequently one lung only is affected. The adhesions may be so extensive that the pleural cavity is almost obliterated, this occurring especially at its upper part. The pleura is much thickened, and fibrous looking, and on the surface of the visceral layer, bluish-grey gelatinous nodules may be observed. On palpation the surface of the lung near the apex feels hard and fibrous, but somewhat irregular, whilst lower down are a number of firm wedge-shaped or nodular masses near the pleura or in the substance of the lung.

On section, the pleura near the apex is found to be greatly thickened—as much as a quarter of an inch, or even more in some cases. Under the thickened pleura, and usually very near the apex, are cavities, one or more in number, each bounded by a firm fibrous wall with a glistening lining, and usually containing a soft caseous looking mass, which partially fills the cavity. These cavities vary greatly in size, “from that of a hazel nut up to that of a small orange.” The fibrous wall of the cavity is deeply pigmented, and appears to be continuous with the thickened pleura. Throughout the whole lobe are bands of fibrous tissue, most numerous around the above

mentioned cavities, but also following the lines of the interlobular septa, the deep layer of the pleura, and the peribronchial and perivascular tissues. In this fibrous tissue are small yellow caseous-looking masses, similar to, and formed in the same manner as, those seen in silicosis (§ 326). The wedge-shaped masses under the pleura are in the form of bunches of grapes, the base of the pyramidal mass being situated towards the pleura. From the apex of the mass, the "stalk" consisting of a line of small round nodules is seen to extend. In the substance of the lung, irregularly rounded masses of similar appearance are met with, packed closely together in the upper part of the lung, but, towards the base, with large highly vascular areas of lung tissue between them. These larger masses are composed of small rounded or ovoid shot-like bodies, firm to the touch, and of a bluish-grey colour; the centre usually is very fibrous and deeply pigmented, the peripheral zone gelatinous and even pink. In some cases the centre, in place of being hard and fibroid, is softened and yellow, but where this is the case the growth appears to have been somewhat more rapid than in the above typical form. Around the bronchi similar masses are seen. These are the so-called tubercle masses, but it must be borne in mind that each of these is not a simple body, but is made up of several tubercle follicles. Around the larger masses are a number of smaller points which are usually surrounded by a pneumonic zone. These changes are always most marked in the upper lobe of the lung, where the solidified patches may have become so fused that they present a solid area, in which, however, are caseous or calcareous nodules the result of degenerative changes; the tissues, of which the solidified parts are composed, are very fibrous and deeply pigmented. In the lower lobe the several tubercle masses are more distinct, have not undergone fibroid or caseous changes, and have more or less congested lung tissue between them.

In some few cases the lower lobe or base of the lung is solidified, yellow, and caseous, and exactly in the condition described as advanced acute phthisis (§ 336). This appears to be quite a secondary condition, and usually occurs in one lung only.

Harden pieces of the lung taken from various points (§§ 56 and 59, 62 or 63), and stain (§§ 102 or 103 and 183 *et seq.*).

($\times 20$ or $\times 50$).—Each nodule contained in one of the grape-like masses is composed of a number of giant cell systems or tubercle

follicles, each of which has the structure previously described (§ 246), the oldest follicles being near the centre, the youngest at the periphery.

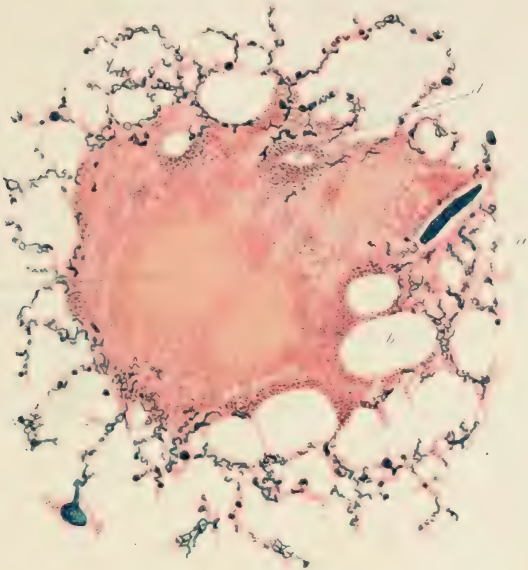


FIG. 156. —Section of chronic tubercle of the lung. Injected with Prussian-blue gelatin. Stained with alum hæmatestin and van Gieson's stain. ($\times 50$.)

- a.* Giant cell in the centre of a tubercle follicle, with a yellow homogeneous centre and a ring of deeply stained nuclei.
- b.* Peripheral cellular zone of a tubercle follicle in which caseation of the central part is taking place.
- c.* Caseating centre of a tubercle follicle.
- d.* Small round cell tissue at the margin of a tubercle nodule.

The whole group of tubercle follicles forms a tubercle nodule.

This tissue is quite avascular, but is surrounded by comparatively healthy vascular (injected) lung tissue.

In the extremely chronic condition the giant cell systems are most perfectly developed at the periphery of the nodule, the central part only rarely being caseous: more frequently, the centre has become quite fibroid, whilst the peripheral fibrous network has become com-

pressed, so as to form a mass of dense fibrous tissue. The younger tubercle follicles around the primary degenerating follicle are readily distinguished by their more typical structure. Under this power observe the positions in which the nodules, caseous and stained yellow, occur in the deep layer of the pleura, in the interlobular and interalveolar septa, and in the peribronchial and perivascular tissues, all of which are greatly thickened. It is a significant fact, as often pointed out, that the tubercle nodules follow very much the same course as the pigmented nodules and pigment injection in the dust diseases, *i.e.* the course of the lymphatics. Note, too, that the tubercle follicles are growing into the air vesicles from the interalveolar septa. These tubercle follicles may be seen in various stages of development. One may be represented by thickening of the septum, in which a number of small round cells and some large endothelioid plates are seen occupying the space around the capillary vessel. At other points the cellular mass appears to be projecting into the air vesicle, pushing the epithelial lining of the wall before it. Usually a giant cell is to be observed in the centre of such a follicle, the centre stained bright yellow, the nuclei at the periphery, crimson. Around the tuberculous nodules are numerous patches in which catarrhal or fibrinous exudation fills the air vesicles. There may be an actual tuberculous growth in the walls of the bronchus, extending into its lumen and diminishing its size, and even causing ulceration of the mucous surface; a similar condition on the walls of the vessel may lead to partial obstruction of its lumen. In addition to these changes in the wall of the vessel, endarteritis obliterans is often present. In these cases acute or croupous pneumonia is more commonly met with than is the catarrhal form.

In a section from a case of phthisical lung in which there were well-developed chronic cavities the arrangement of the elastic tissue enables us to follow the course of the disease rather more accurately than in most other forms.

($\times 50$).—The fibrils of elastic tissue mark out, even in places where caseation is far advanced, the interalveolar septa. In some cases the catarrhal cells filling these alveoli may still be seen, whilst in others the caseation has removed all cell outline and there is simply a homogeneous mass very imperfectly stained, the stained elastic tissue indicating the position of the walls of the alveoli. The granulation tissue which forms the wall of one of the chronic phthisical cavities,

like the new cellular inflammatory tissue which surrounds the blood vessels, contains practically no elastic fibre. From this it will be gathered that it is only where we have a rapid breaking down and discharge of a caseous mass that we should expect to find the elastic tissue in the sputum, and that where we have simply the discharge coming from the wall of a cavity consisting of granulation tissue, no such elastic tissue will be met with. Note the proliferation of the tunica intima and the obliterative endarteritis. The lumen of the vessels in

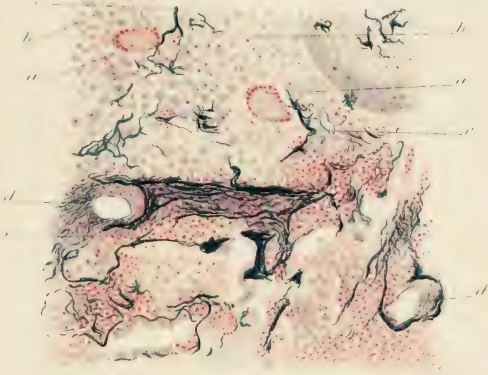


FIG. 157.—Section of lung affected with chronic tubercular phthisis. Stained by Weigert's elastic tissue stain and alum carmine. ($\times 100$.)

- a.a.* Giant cells in the centre of tubercle follicles.
- b.b.* Endothelioid cells, etc., of tubercle follicles.
- c.c.* Bundles of yellow elastic fibre lying close to giant cells.
- d.d.* Small arterioles, with fairly well-marked endarteritis.
- e.* Proliferating adventitia (due to invasion of perivascular lymphatics by tubercle bacilli).

these cases may be almost completely occluded by this endarteritis, the circulation, however, being partially carried on by smaller vessels which grow in the new tissue, some of these, it is said, developing an elastic coat of their own.

($\times 300$).—Observe the tuberculous and fibroid masses in the deep layer of the pleura, in the interlobular and interalveolar septa, and in the peribronchial and perivascular tissue. In the wedge-shaped patches of tubercle near the surface, the individual nodules, each surrounded

by pneumonic zones, should be further examined; these patches may be taken as typical of the patches found throughout the lung, with the exception of those at the apex, where fibroid changes are more marked.

Each patch is made up of tubercle nodules, which again are composed of tubercle follicles. In the centre of the nodule are masses of granular débris, in which are a few angular and shrivelled cells, with here and there fatty globules or granules, stained black by osmic acid (§ 135). Around the central mass, which is simply caseous tubercle, is

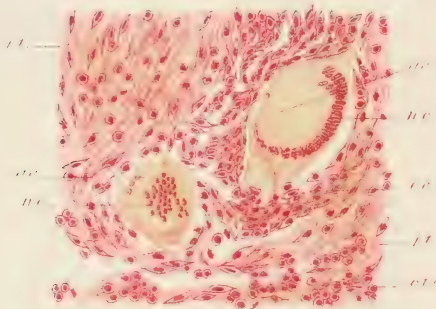


FIG. 158.—Giant cells from a case of chronic tuberculosis of the lung. Stained with picro-carmine. ($\times 300$.)

g.c. Branching giant cells with yellow homogeneous basis.

n.c. Nuclei of giant cell.

e.c. Endothelioid cells lying on the delicate network around a giant cell.

f.t. Fibrous stroma, here more fully formed, comparatively few endothelioid cells near the periphery, but a considerable number of smaller and rounded (*c.t.c.*) cells are seen. These are simply such cells as are seen in rapidly proliferating connective tissue.

a zone of tubercle follicles, each of which has the regular giant cell structure. Farther out again is a zone in which are tubercle follicles, growing principally into the air vesicles, and usually accompanied by pneumonic exudation. Examine one or two of the tubercle follicles in the interalveolar septa, the endothelioid cells of various forms and sizes, and the small round cells, all formed by proliferation of the endothelium of the lymphatics and of the connective tissue cells. As this mass grows it is seen to make its way into the air vesicle, pushing before it a regular layer of epithelium, which afterwards desquamates and degener-

ates as the connective tissue grows further into the vesicle: the giant cell makes its appearance and the tubercle follicle is developed. Around the tubercle nodules there is, as seen above, an inflammatory exudation—croupous or catarrhal, especially in the more acute forms.

Tubercle bacilli are much more rare in chronic phthisis than in the more acute process, but they may be found in the specially stained specimens, particularly during the earlier stages of the disease. They must be looked for with a high power ($\times 600$) in the lymph spaces, where the cell proliferation is taking place most rapidly.

In the "Weigert"-stained specimen the elastic tissue may be seen close to the giant cells, though much of the new tuberculous tissue contains no trace of elastic fibre. In the walls of even small blood vessels, as also in the interlobular septa, the elastic tissue may still be seen.

In exceedingly chronic tubercle (fibroid) there may be only slight surrounding inflammatory changes, the giant cell participating in the fibroid change, and the process becoming quiescent.

The bronchial glands, on microscopic examination, are found to be tuberculous,—pigmented, fibroid, and, frequently, caseated.

ELASTIC TISSUE IN SPUTUM

338. Before concluding this short description of the pathological conditions of the lung, it may not be out of place to say a few words as to the treatment of sputum (the contents of phthisical cavities, etc.), in order to demonstrate the presence of the elastic membrane of the alveolar walls and other elastic tissue, which, as we have seen, resists pathological disintegration far longer than most of the tissues.

To separate the elastic tissues Fenwick's method is undoubtedly the best. He boils the sputa in a beaker with an equal quantity of a strong solution (at least 20 grains to the ounce) of caustic soda or potash, until all the mucin and cement substance are dissolved. A quantity of water is then added to the fluid, and the whole is put aside to sediment in a conical glass. All other tissues are dissolved or separated, but the elastic fibres remain unaffected; they sink to the bottom of the glass, whence they may be removed by means of a pipette, transferred to a slide, and examined. The elastic fibres are seen as translucent, curled yellow fibres, sometimes in regular bundles, at others in short fragments. Their peculiar "curliness" is their chief characteristic.

In certain cases crystals are met with in sputa, especially long,

delicate, colourless, acicular, fatty acid crystals, which are sometimes mistaken for elastic fibres; they may, however, be easily differentiated by the addition of ether, which dissolves fatty acid crystals, but does not affect elastic fibres. Charcot's crystals, which are met with in cases of asthma and chronic bronchitis, are delicate, colourless, long, and spindle shaped. They are soluble in dilute acids or alkalies, but are unaffected by alcohol. Various other disintegration crystals, such as cholesterin, leucin, tyrosin, and hæmatoidin, may also occur in the sputum.

OTHER PATHOLOGICAL CONDITIONS MET WITH IN THE LUNG

339. Pyæmic abscess is sometimes met with in connection with a general condition of pyæmia. In such a case the abscesses are near the surface, and over the inflamed and degenerating tissue there is usually acute pleurisy. Similar small abscesses are sometimes met with where there has been pressure on a bronchus, by an aneurism for instance, leading first to pneumonia and pleurisy, and, ultimately, to small abscess formation.

Harden (§ 59, 62, or 63) a piece of the lung containing a small abscess—near the pleural surface if possible, stain (§ 115 or 173), and mount (§§ 193 and 199).

($\times 50$).—Examine the vessels in the deep layer of the pleura and near the abscess. They and the lymph spaces in the neighbourhood are distended, and in them masses of micrococci are found.

The centre of the abscess may be recognised by the yellow staining of the tissue and lack of nuclear staining; the outlines of the alveoli are faintly distinguishable, but the tissue is evidently in an advanced stage of acute necrosis. Small collections of leucocytes may still take on the nuclear stain. At the margin of this "dead" area are masses of micrococci multiplying, apparently, in the vessels to which septic emboli have been carried. Around the dead (digested) tissue are numerous polymorpho-nuclear leucocytes along with a few large mono-nuclear cells and a larger number of lymphocytes. This infiltration with leucocytes may be so marked that it is difficult to make out any lung tissue at all. Immediately outside this cellular zone is an area in which the alveoli, somewhat collapsed, contain a quantity of fibrinous lymph with a few nuclei; some in cells derived from the epithelium, some in those from the connective tissue or from the interalveolar

blood vessels which are dilated. The air vessels around this zone are much more distinctly outlined, and although the interalveolar vessels



FIG. 159.—Section of a small pyæmic abscess of the lung. Stained by Gram's method, counterstained with alum hæmatein and van Gieson's stain. ($\times 50$.)

- a.* Centre of an abscess in which the tissues are necrosed and digested.
- mic.* Masses of micrococci, some of them contained in blood vessels (embolic).
- p.c.* Zone of polymorpho-nuclear and other cells. (So-called pyogenic area.)
- coll.v.* Collapsed air vesicles, some containing coagulated fibrin, others catarrhal cells and leucocytes.
- v.* Congested blood vessels.
- alv.c.* Air vesicles, not so small and containing large numbers of catarrhal or proliferating epithelial cells.

are distended and congested, the air space is fairly well defined, and contains a large number of catarrhal cells and a few leucocytes, but little fibrin.

($\times 300$).—The pus cells at the margin of the abscess are seen to



FIG. 160.—Section of small pyæmic abscess of the lung. Stained by Gram's method, counterstained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- mic.* Micrococci in the wall of an abscess.
- p.c.* Polymorpho-nuclear leucocytes, many with pyknotic changes in the nucleus.
- m.* Mononuclear cell the same cell (?) as
- cat.* The proliferating cells in a small alveolus.
- fib.* Fibrin and polymorpho-nuclear cell in neighbouring alveolus.
- e.p.c.* Large cell derived from the epithelial lining of an alveolus.
- v.* Congested vessels with well-marked endothelial lining in the interalveolar septa.
- r.b.c.* Red blood corpuscles that have escaped, along with plasma and leucocytes, into an alveolus.

be made up of polymorpho-nuclear leucocytes of which the nuclei are

undergoing disintegration (pyknosis), of a few large mononuclear cells derived either from the epithelium lining the air vesicles or from the connective tissue. The congested interalveolar vessels, the fibrin, and the catarrhal cells of the "zones" surrounding the abscess are readily made out.

In farcy, there are often evidences of catarrhal pneumonia, fat embolism of the lung, etc., and small bacilli are also described both around air vesicles and bronchi. Small abscesses are met with in actinomycosis; in or near which the characteristic mycelial fungus is usually found. (See §§ 251 and 502.)

ANIMAL PARASITES MET WITH IN THE LUNG

340. *Hydatids*, *Filaria bronchialis* (especially in sheep), and sometimes, but rarely, the *Cysticercus cellulosæ*.

PRIMARY TUMOURS OF THE LUNG

341. *Lipoma*, *osteoma*, and *fibroma*, the latter especially near the bronchi, are sometimes met with.

Chondroma or *enchondroma* occurs in connection with the bronchial cartilages.

Cylindrical or *columnar-celled epithelioma* grows as a primary tumour in connection with the bronchial glands and ducts.

Squamous epitheliomas are also described, but are very rare.

SECONDARY TUMOURS OF MALIGNANT TYPES

342. Ziegler says of secondary tumours in this position, that "examples of every tumour that gives rise to metastases at all, have been found in the lungs." Of these, from the extreme vascularity of the organ, the most common are the *sarcomas*, especially the more malignant forms. (See § 452 *et seq.*)

The *melanotic sarcoma*, which appears as a somewhat flattened or rounded mass, immediately below the pleura, is deeply pigmented: its structure is similar to that of the same sarcoma as it occurs in other positions.

The same may be said of the other forms of sarcoma as regards structure, but these occur much more frequently in the substance than near the surface of the lung.

Lymphosarcoma, *lymphadenoma*, which usually spread from the mediastinum.

Small round-celled sarcoma, and *small spindle-celled sarcoma*, *osteoid*, and *myeloid sarcomas*.

Malignant enchondroma, secondary to the same condition in the testicle.

Myxochondroma, secondary, in one case, to myxochondroma of the periosteum of the scapula (Greenfield). This is met with as semi-gelatinous bluish cartilaginous masses in the branches of the pulmonary artery, the branchings of which they follow closely (§ 309).

Cancers — *scirrhus*, *encephaloid*, *colloid*, and *adenoid* (or the columnar-celled epithelioma), and *squamous epithelioma* (which is usually secondary to that of the tongue, when it spreads through the mediastinal glands).

Any of these forms of cancer may occur in the lung, as there is a very free distribution of lymphatics and lymphatic glands in this organ and in its pleural covering. They are almost invariably multiple. It is somewhat difficult to distinguish them from the sarcomas in this position, especially in the earlier or softer forms; but later, and in the harder forms, puckering of the pleura and umbilication occur, just as in scirrhus cancer of the breast. Microscopically they resemble the same tumours in other organs. (See Chapter XIV.)

CHAPTER IX

THE SPLEEN

NORMAL HISTOLOGY

343. The spleen is a flattened, somewhat crescent-shaped organ, from 5 to $5\frac{1}{2}$ inches (12.5 to 14 cms.) in length, 3 to 4 inches (7.5 to 10 cms.) across, and 1 to $1\frac{1}{2}$ inch (2.5 to 3.75 cms.) in thickness; these measurements vary considerably in different cases. The weight is usually from 5 to 7 oz. (140 to 200 grms.), though this also may vary considerably, as, "even when perfectly free from disease, it may fluctuate between 4 and 10 oz." (110 to 280 grms.) (Quain's "Anatomy"). The anterior margin is notched; these notches persist, however large the organ may become. On the concave surface of the spleen is a vertical fissure, termed the hilum, at the bottom of which are numerous openings, where the blood vessels enter and emerge.

Investing the organ is (1) a serous coat, which is simply a reflection of the peritoneum. This forms a capsule, and is covered with a layer of flattened endothelial cells which, seen in section, are spindle-shaped. Beneath this is (2) a layer of connective tissue, in which are elastic fibrils. Beneath this again is (3) a denser mass of connective tissue, in which are blood vessels, nerves, and a few non-striped muscle fibres. Running in from the hilum on the one hand, and from the deeper layer of the capsule on the other, are numerous septa or trabeculae, composed of connective tissue and of bands of non-striped muscle fibre, evidently continuous with those of the capsule. These trabeculae divide and subdivide until the ramifications become very small, and the terminal filaments of the trabeculae from the capsule, meeting those from the hilum, form a supporting framework of connective tissue.

The arteries of the spleen enter at the hilum, and together with

the veins run along the fibrous trabeculæ, in which position there are numerous perivascular lymphatics. The artery soon leaves the vein, and at once breaks up into a tuft or pencil of small arterioles. These leave the trabeculæ, and are continued into the splenic substance proper. After leaving the fibrous trabeculæ, each arteriole is invested with a mass of tissue known as an adenoid sheath (a largely developed perivascular lymphatic tissue), a beaded-looking column with irregular enlargements, bulgings, and constrictions, in which the artery is usually placed somewhat eccentrically. This column with the artery in or near

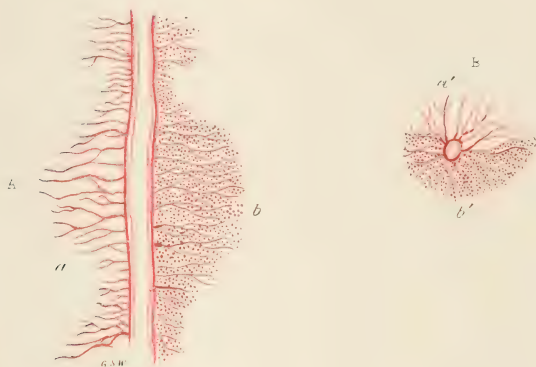


FIG. 161.—Diagram representing the arrangement of the capillary vessels in the adenoid sheath (Malpighian corpuscle).

- A.* Longitudinal section of the arteriole, with its sheath.
- B.* Transverse section.
- a, a'.* The capillary vessels which convey the blood from the small arterioles to the splenic sinuses.
- b, b'.* Adenoid tissue between these capillary vessels.

the centre, seen in transverse section, is the so-called Malpighian corpuscle. It is composed of a reticular stroma, lying on the strands of which are endothelioid cells, and in the spaces numerous small round corpuscles or lymph cells. This tissue is very dense, and even under the naked eye is usually readily seen, as are also the fibrous trabeculæ. Proceeding from the central artery are "elongated meshes of capillary blood vessels," which run nearly at right angles to the long axis of the sheath, until they come to its margin, when they open out into

the pulp tissue, first into a series of small (arterial) sinuses (see Fig. 168), and then into larger venous sinuses, from which the blood is collected into the venous trunks, and carried from the organ along the trabeculæ to the hilum, and thence to the portal vein.

The splenic pulp—the tissue in which the adenoid sheaths or Malpighian corpuscles are embedded—is composed of a mass of tissue of sponge-like structure, in which are small open spaces communicating with the capillary vessels as they emerge from the adenoid sheath: they are bounded by large transparent endothelial cells or plates, containing one or more large nuclei, and lying on a trabecular tissue. In the sinuses themselves are numerous lymphoid cells, in which, as well as in the endothelial cells, blood corpuscles, or pigment derived from them, are frequently found embedded. There may be a few large cells partially attached to the epithelial cells by stalks or pedicles (the cells proliferating by budding). Opening out from these smaller sinuses of the pulp are larger tubular sinuses, lined with similar endothelial cells, and containing large and small nucleated cells (Figs. 163 and 168), and usually some coloured blood corpuscles. Supporting the walls of the larger sinuses are bands or fibrils of yellow elastic tissue, which are arranged almost like barrel hoops. From these larger or venous sinuses the blood is poured into the venous trunks.

Harden a section of a healthy spleen (§ 59, 62, or 63), stain (§ 102 or 104), and mount (§§ 195 or 193 and 199).

(× 50).—Note the capsule with the trabeculæ running at right angles to it. Between the trabeculæ the rounded masses of denser looking tissue appear to be made up of small lymphoid cells. These denser masses are Malpighian corpuscles; they vary considerably in size and shape, according to the direction in which the section through the adenoid sheath is made,—rounded if cut transversely, oval if cut obliquely, and elongated, or even bifurcated (at the point of bifurcation of a vessel) if cut vertically; the size varying according as the section passes through an enlarged or a constricted part of the sheath. The vessel is usually situated at some distance from the centre, and may even be near the margin of the sheath. Surrounding the Malpighian corpuscles (sections of the adenoid sheaths) the splenic pulp is recognised as a spongy open network, containing sinuses of various sizes, those nearest the Malpighian corpuscles being considerably smaller than those further away. Running through the splenic pulp, as will afterwards be better observed in the waxy spleen, are numerous

small arterioles, which apparently are not in direct communication with the arterioles of the Malpighian corpuscles.

($\times 300$).—The various features above described must be observed, and special attention paid to the capillaries in the Malpighian corpuscles, the lymphoid tissue of which these corpuscles are composed, the arterial sinuses, with their endothelial lining, the large round and nucleated cells, the smaller lymphoid cells, and the coloured blood corpuscles. Note the similar structures in the large venous sinuses, and the encircling elastic bands in their walls. Examine also the connective tissue and non-striped muscle fibre in the trabeculæ.

ACTIVE HYPERÆMIA OF THE SPLEEN

344. In this condition the spleen undergoes changes which are very evident to the naked eye, but, under the microscope, are less characteristic.

Hyperæmia is usually associated with continued high temperature in septic, specific, and malarial fevers, and in syphilis. The organ is enlarged, in some cases to two or three times the normal size, and the capsule is stretched. On section the substance is soft, diffuent, contains much blood, and is of a dark red colour, which turns to a bright arterial red when the cut surface is exposed to the air for a few minutes. In the more acute septic conditions, such as typhus fever or acute septicæmia, the hyperæmia is more acute, and the tissue, especially in the early stages of the disease, is bright red or even pink, when the organ is first cut into; if the patient lives for a time, the tissue still remains soft, but it becomes paler and almost creamy, and the trabeculæ and Malpighian corpuscles are not nearly so prominent as they lie in the mass of soft creamy-looking pulp.

In the most acute form, *i.e.* that met with in malarial fevers, the enlargement may be so great and so rapid that the spleen may actually rupture.

In small-pox, scarlet fever, and typhoid fever, especially in the later stages, the spleen, instead of being diffuent, may be comparatively firm. In such cases it may be enlarged even to as much as four times its normal size. The Malpighian corpuscles are considerably increased in size, owing to swelling of the adenoid tissue. The whole surface has a peculiar greyish or sometimes yellowish tinge mixed with the red.

This active hyperæmic stage may be followed by a stage of resolution, as seen in a spleen taken from a case of acute pneumonia, in which death supervened during the stage of grey hepatisation or early resolution. The organ is considerably smaller than normal, the pulp appears to be greatly diminished in volume, and the trabeculæ stand out very prominently as white fibrous bands passing in from a somewhat thickened and greatly wrinkled capsule.

Harden (§ 58, 63, or 68), stain (§§ 102, 103, or 110 (*b*) and 132), and mount (§ 195 or 199).

($\times 50$).—The most prominent feature is the increased quantity of blood in the pulp sinuses; scattered throughout these are numerous leucocytes. The Malpighian corpuscles are enlarged, though this enlargement cannot always be recognised, as, relatively to the increased pulp, the corpuscle may be smaller. The small round lymphoid cells are numerous, and take on nuclear stains very readily. Where the Malpighian corpuscles stand out prominently, as in diphtheria, typhoid, and scarlet fevers, this increase in the amount of adenoid tissue becomes a very marked feature in the field of the microscope. Along the lines of the smaller trabeculæ there is frequently proliferation or exudation of leucocytes deeply stained, the result of inflammation and increased blood pressure.

($\times 300$).—When the congestion is comparatively simple, little more can be made out than distension of the sinuses with red blood corpuscles, with here and there a few colourless blood corpuscles and a number of larger nucleated cells, which appear to be derived from the proliferating endothelial cells which line the pulp sinuses. These endothelial cells are all swollen, and appear cloudy; some contain several nuclei, and others a number of red blood corpuscles, or a quantity of golden-brown pigment, which is evidently derived from these blood corpuscles. In the adenoid sheath of the vessel the lymphoid corpuscles are numerous, and, in addition, the endothelioid plates, lying on the trabeculæ of the adenoid network, are increased in number; this is not nearly so marked as in those cases in which there is definite inflammation, where, also, the changes in the trabecule and sinuses are more distinct. Rapid proliferation of the endothelial cells takes place, and consequent accumulation of leucocytes in the sinuses, migration of leucocytes along the lines of the trabeculæ in which the vessels run, and other evidences of an inflammatory condition ensue. As a result of this, abscesses may form, especially

in or near the Malpighian corpuscles, where there is rapid accumulation of leucocytes, pus formation, and general breaking down of the tissue elements. The abscesses may appear as small yellow points on the surface of a section; more frequently they are single and are of larger size. In many cases they are of septic embolic origin, as in acute ulcerative endocarditis, pyæmia arising from whatever cause, and typhoid fever. Such abscesses run an acute course, beginning as dark red hæmorrhagic-looking patches, which rapidly undergo suppurative changes.

CHRONIC CHANGES

345. In cases in which the febrile condition is prolonged, or where there are repeated attacks, as in malarial fevers, the spleen may become permanently enlarged. It is then firm, and of a dirty greyish-red, with pigmented patches seen through the capsule. On section the capsule is thickened, and running from its deeper layer are numerous thickened trabeculæ. The Malpighian corpuscles may also be enlarged, though it is often very difficult to distinguish them from the surrounding firm pulp tissue, which is very brittle, and not nearly so full of blood as in the normal condition; whilst scattered over the whole of the surface, evidently the result of pigmentation, are grey or even black patches. In malarial disease the pigmentation is more marked than in any other chronic form of enlarged spleen; but enlargement and fibroid change may be noted in a variety of conditions, not only in those mentioned above, but in rickets, congenital syphilis, or, more rarely, in the later stages of acquired syphilis.

Harden (§ 60, 62, or 63), cut (§ 82 *et seq.*), stain (§ 102, 103, or 110 (*b*)), and mount (§§ 195 or 193 and 199).

($\times 50$).—Note the thickening of the capsule and of the fibrous trabeculæ, and the increase of the adventitia of the vessels. The pulp tissue is altered, the spaces are not necessarily larger—frequently they are even smaller than normal—but their walls are thickened. The adenoid sheaths of the arteries—the Malpighian corpuscles—are more fibrous in appearance, and the number of small round lymphoid cells is in many cases considerably diminished. At the margins of the adenoid sheaths and in the pulp proper are numerous accumulations of golden-brown pigment embedded in the fibrous tissue or in the cells.

($\times 300$).—Observe the thickening of the fibrous capsule and of the trabeculae, and the elongated or rod-shaped nuclei of the hypertrophied bands of muscle fibre. The Malpighian corpuscles are more fibroid, and large quantities of dark altered blood pigment

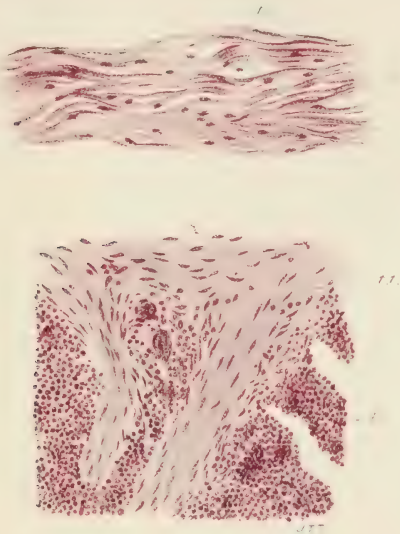


FIG. 162.—Drawing of spleen with chronic fibroid thickening of the capsule and trabeculae. Stained with magenta. ($\times 200$.)

- f.c.* Fibroid thickening of the capsule (flat fibroma).
- n.* Connective tissue nuclei.
- c.* Deep layer of the capsule in which are elongated nuclei, some of which are nuclei of non-striped muscle fibres.
- t.t.* Thickened trabeculae prolonged downwards from the deep layer of the capsule to which they are similar in structure.
- p.* Splenic pulp.

may be seen at their margins. Note the thickened walls of the pulp sinuses, in which the endothelial cells often contain large quantities of blood pigment, as do also the rounded cells lying free in the sinus. There may also be considerable pigmentation of the tissue, of which the walls of the sinuses are composed.

CHRONIC VENOUS CONGESTION OF THE SPLEEN

346. Another form of chronic interstitial thickening is due more directly to mechanical causes. This is met with wherever there is any obstruction to the outflow of venous blood from the spleen. It is found in cases of long-standing heart disease, especially of the mitral valve; in common cirrhosis of the liver, where there is obstruction to the portal circulation; in fibroid phthisis and emphysema, where there is impeded flow of blood through the lungs, and consequently impaired systemic venous circulation; or where there is direct pressure upon the splenic vein.

The chronic venous congested spleen is usually slightly enlarged. It is also heavier, firmer, and more fleshy than normal. The capsule is thickened, and, like that of the liver in the corresponding condition, may have villous projections or hard cartilaginous patches on its surface. The cut surface presents a peculiar fleshy appearance, and a bluish-red or purple colour; and although there may be thickening of the trabeculae, there is no evidence of this to the naked eye. The edge of the cut section is sharp and well defined.

Harden (§ 62 or 63) and stain (§§ 102, 103, or 104, and 110 (*b*)).

($\times 50$).—The changes are essentially the same as those met with in similar conditions in other organs—nutmeg liver (§ 238), chronic venous congestion of the kidneys (§ 286) or lungs (§ 329).

The venous sinuses are distended with blood, and thus occupy a considerable part of the section. From the splenic pulp the fibrous trabeculae stand out very prominently, but the adenoid sheaths are not so readily distinguished as in the normal condition. They are more fibroid, and the lymphoid cells are not so numerous. The walls of the vessels are usually somewhat thickened. The cellular elements of the pulp are obscured, but delicate strands of fibrillated tissue may be seen running through the section in the walls of the enlarged venous sinuses.

($\times 300$).—The venous sinuses are greatly distended. In them lie numerous coloured corpuscles, with here and there phagocytic polymorpho-nuclear leucocytes in which are granules of altered blood pigment. The flattened endothelial cells lining the venous sinuses also contain altered blood pigment. Between the sinuses there frequently appears to be very little tissue, but careful examination reveals the existence of fibrous strands, on which rest the lining endothelial cells. The

Malpighian corpuscles contain more fibrous tissue than usual, and fewer lymphocytes are seen. Perhaps the most marked changes are



FIG. 163.—Chronic venous or passive congestion of the spleen.
Stained with logwood. ($\times 300$.)

- a.* Large pulp sinus cut longitudinally, lined with flattened nucleated endothelium, and filled with red blood corpuscles, with here and there a deeply stained leucocyte.
- b.* A similar sinus seen in transverse section. Large mononuclear cell seen lying in the centre.
- c.* Small sinuses.
- d.* Vessel in the centre of (*e.*) a Malpighian corpuscle. The walls of the vessel are somewhat swollen, and the adventitia hyaline. The lymphoid and other cells of the adenoid sheath (Malpighian corpuscle) are well seen.
- f.* Around the sinuses in this position there are regular accumulations of small round cells in the walls.

in the fibrous trabeculae, which appear to be considerably thickened, and around the vessels running in them are usually a number of

leucocytes. There is also fibroid or cartilaginoid thickening of the capsule (Fig. 162). These latter are merely masses of fibrous tissue (the flat fibroma described in § 434). The villous projections are young masses of connective tissue or granulation tissue, with a quantity of coagulated fibrin on the surface. In the trabeculae and in the capsule there is also marked hypertrophy of the muscular tissue, the elongated nuclei of which can be easily distinguished.

EMBOLIC INFARCTION OF THE SPLEEN

347. An infarct is the area of tissue supplied by a terminal artery the small vessels of which are "stuffed" with stagnant blood, which is unable to supply nutriment to the tissues; these tissues rapidly undergo degenerative changes. In the spleen, infarction occurs in its most typical form. It will therefore be well to take the description of this condition from the appearances here presented.

In its earlier stages the infarction appears as a slight projection running transversely across the convex surface of the enlarged spleen; it is usually deep purple or brick-red throughout, according to the stage which it has reached; it is firm, and, on palpation, readily defined from the surrounding softer splenic tissue; it may pass for a considerable distance into the organ, or it may involve a superficial patch only. On section it is found to be wedge-shaped, with a rounded base at the capsule, the apex pointing towards the hilum. The surrounding pulp is usually highly congested. Of these wedge-shaped masses there are usually three, four, or more, but there may be only a single one involving a large section of the organ. Examined at various later stages, the centre becomes paler; then a yellowish pallor spreads towards the periphery, until the whole mass, with the exception of a zone at the outer margin, is completely involved. This outer congested zone persists for a considerable time, and eventually in this position there is formed a capsule of fibrous tissue, which, as it becomes more and more cicatricial, slowly retracts, and draws on the capsule at the margins of the infarct, and a kind of fossa or depression is formed around the yellow fatty mass. Following fatty degeneration, absorption and caseation set in. If the process of absorption continues, the whole of the necrosed tissue may be removed, when there is left, to mark the position of the infarct, merely a fibrous cicatrix. In many cases, however, all that remains is a cyst, or a

cheesy or calcareous mass, surrounded by the retracting fibrous capsule.

Harden (§ 58, 60, 62, or 63), stain (§§ 102, 103, or 110 (*b*) and 132), and mount (§ 193 or 199).

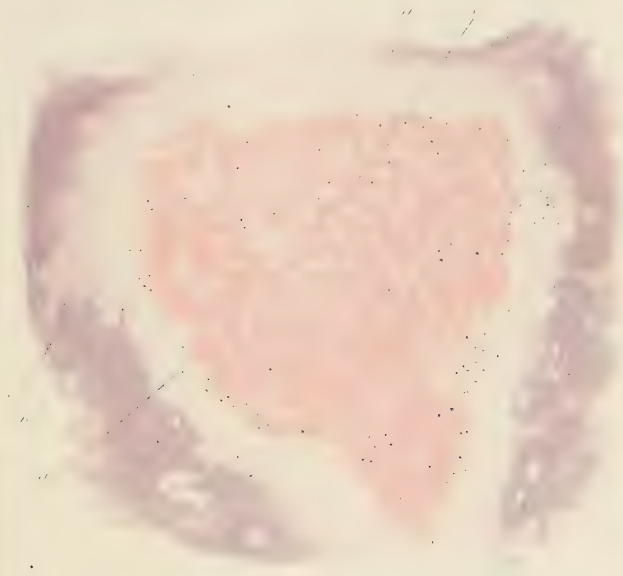


FIG. 164.—Section of a small infarct of the spleen. Stained with eosin and logwood. ($\times 20$.)

- a.* Surface of spleen.
- b.* Fibrous capsule formed within
- c.* Congested zone.
- d.* Pigmented cells, etc., most numerous in the inner layers of the fibrous capsule.
- e.* Pulp sinus with swollen and degenerating walls. The dead splenic tissue in which the infarction has taken place.

($\times 20$).—In a section taken from a very early infarct there is little to be seen beyond an enormous distension of the various vascular channels and sinuses. At a later stage fatty degeneration of the various tissues supervenes, especially towards the centre of the

infarct: this is readily observed in a section stained with osmic acid (§ 135). At the periphery of the swollen mass in the position of the hyperæmic zone there is an enormous accumulation of leucocytes or young connective tissue cells. Later these latter cells are organised into connective tissue, which, becoming more and more fibrous, forms bands of fibrous tissue; these run up to a puckering in the capsule, around the caseous mass, in which, at this stage, pigment granules, and fatty granules and globules, are the principal constituents; but crystals of cholesterin, hæmatoidin crystals, some fat crystals, or even calcareous salts, may also be found. The lime salts disappear with the evolution of gas bubbles on the addition of hydrochloric acid. Pigment granules are also to be seen in the fibrous capsule, especially near its inner surface. The capsule of the spleen frequently presents evidences of localised inflammatory thickening over the infarct.

($\times 300$).—Confirm the above. In the centre of the area the degenerating tissues are seen as ghosts, whilst at the margin the granulation tissue, often deeply pigmented, can be seen to correspond with that in other positions.

WAXY SAGO SPLEEN

348. Waxy degeneration occurs more frequently in the spleen than in any other organ in the body, with the sole exception of the kidney. It assumes one of two forms—(1) the “sago” waxy spleen, and (2) the diffuse waxy spleen. In the first the process is confined principally to the adenoid sheaths of the vessels—the Malpighian corpuscles; in the second the pulp is the part specially affected. A careful examination of these two forms of waxy spleen will enable the student to understand the structure of the spleen, and to note the part which the various elements play not only in this, but in other pathological processes. For this reason a somewhat detailed account of waxy disease is here given.

In the sago form, the spleen is usually, though not invariably, somewhat enlarged; it is firm and elastic, and in this respect resembles the liver and differs from the waxy kidney. On section, the general appearance varies in different cases. Sometimes, where there is a large quantity of blood in the organ, it is red, and the Malpighian corpuscles appear as dark shining masses studding the surface. In other cases the pulp is paler, and then the Malpighian corpuscles also

appear lighter in colour; they are transparent and gelatinous in appearance, and have been aptly compared to grains of boiled sago, which, on the addition of iodine (§ 133) give a mahogany-brown reaction; the surrounding healthy tissue then giving a yellow colour.

Harden (§ 58 or 60), mount one section unstained (§ 195), stain others (§§ 117, 133, and 134).

($\times 50$).—Each Malpighian corpuscle is stained red violet, with the

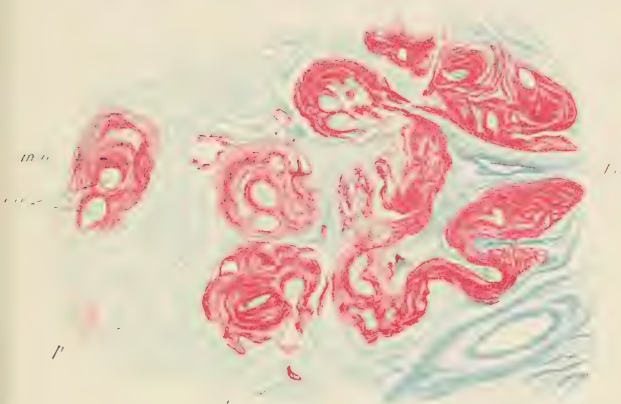


FIG. 165.—Waxy sago spleen. Stained with methylanilin-violet.
($\times 30$.)

- l.a.* Large arteriole, giving off branches around which the waxy adenoid sheath is readily seen.
- m.b.* Malpighian body or adenoid sheath with (*c.a.*) its healthy arteriole in the centre; the two seen here are evidently near the point of bifurcation of the arteriole.
- a.* Small waxy vessel in the splenic pulp.
- p.* Splenic pulp.

exception of a small blue ring in the centre, surrounded by a thin zone of blue tissue. Where the condition is advanced, the red violet mass appears to be almost homogeneous; but near the central blue patch—the unaffected larger central artery of the adenoid sheath—or at the periphery of the sheath at its junction with the splenic pulp, delicate red lines may be seen running from the solid violet mass into the surrounding blue tissue. The central blue ring is surrounded by a thin zone of comparatively healthy adenoid tissue. Around the waxy

Malpighian corpuscle the splenic pulp (sinuses, cells, and vessels) is at first sight unaffected, and is stained blue, but running from the margins of the waxy mass are small capillary vessels, the walls of which are undergoing the waxy change—the thin red violet lines already mentioned. A more careful examination of the splenic pulp, however, reveals a few small red violet lines, rings, and dots running through it. These are evidently sections of waxy blood vessels—small arterioles. In an iodine-stained section, examined by reflected light, the parts seen above as red violet now appear brown, whilst the blue parts are canary yellow in hue. In an unstained section the waxy portions are glistening, translucent, and hyaline, and have a faint yellow tinge.

($\times 300$).—Unless the waxy condition be very far advanced, the walls of the central artery of the Malpighian corpuscle are quite healthy and are stained blue; the intima is thrown into folds by the contracting muscular coat, from which it may be inferred that the muscle is functionally as well as optically healthy. As yet, too, there is no change in the adventitia, and it is only at some little distance from the vessel that any is noticeable. The “degeneration” begins in the walls of the small vessels, which run through the Malpighian corpuscle. These vessel walls are seen as thin, homogeneous, red violet lines, between which the lymphoid cells, stained blue, stand out prominently. Further away from the centre, the vessels are more affected, and not the vessels only, but the delicate strands of fibrillated tissue which compose the network of the adenoid sheath. The strands are swollen and homogeneous, and are stained red violet. Most of the lymphoid cells between them are comparatively healthy, and are stained blue; but where the condition is very far advanced some of these cells appear to be waxy, though it may be that the swollen vessels and fibres have, by pressure, caused them to become atrophied. Certain it is that the cells are not at all readily distinguished. At the periphery of the Malpighian corpuscle, the delicate waxy bands are more readily made out, and the process may be seen to extend for a short distance in the walls of the vascular sinuses beyond it, where there is a condition very similar to that met with in diffuse waxy spleen.

Running through the blue splenic pulp are numerous small arterioles, the walls of which are in an advanced stage of waxy degeneration; the walls of some of the sinuses may also be slightly affected. Where this waxy change in the wall of the sinus has once set in, there

is usually fatty degeneration of the endothelial cells lining the wall of the sinus.

In this position, perhaps, better than in any other, the waxy change in the vessel may be seen.



FIG. 166.—Waxy sago spleen. Stained with alum hæmatein and van Gieson's stain. ($\times 70$.)

Enlarged Malpighian corpuscle, in which the thickened waxy arterioles may be seen stained pink. Within these the red blood corpuscles are well seen.

a.a'. Central vessels, just after bifurcation; these are not waxy.

b. Splenic pulp unaffected by the waxy disease. Here the sinus, lined with endothelium and containing red blood corpuscles, are well seen.

Note (*a*) that the waxy change is confined to the middle coat, especially during the early stage of the disease; (*b*) that the middle coat is picked out in patches by the disease; (*c*) in these patches the tissues are not affected throughout, for on careful examination it will be seen that only between the muscle fibres does the waxy change make its appearance, the longitudinal or transverse

sections of the muscle fibres being stained blue, whilst between them are red violet streaks,—the swollen connective tissue fibrils (see Fig. 94, p. 352).

At the margin of the Malpighian corpuscle the walls of the sinuses are affected, but not extensively. In the pulp the small arterioles and the walls of a few of the sinuses are waxy. As these become more and more swollen, the muscle fibres are atrophied by pressure, and ultimately they may be obliterated. Later, the intima is involved, but the endothelial lining of the vessels then becomes granular and fatty, never waxy. Here, then, is a condition in which the waxy disease affects specially the walls of the small arterioles soon after



FIG. 167.—Drawing of small capillary vessels and connective tissue fibrils undergoing waxy degeneration. Stained with iodine and sulphuric acid. ($\times 600$, after Kyber.)

These vessels were isolated by pencilling from one of the affected Malpighian corpuscles.

The degenerate parts are stained blue; the unaffected connective tissue fibrils and capillary walls are stained yellow.

they are given off from the large central arteriole, then the connective tissue fibrils around them, and it is possible that the lymphoid cells may ultimately be involved, though this does not often occur.

DIFFUSE WAXY SPLEEN

349. It is often stated that this is an advanced form of the foregoing, but such is not by any means usually the case. Where it is simply an advanced sago spleen, the Malpighian bodies are most markedly affected, and the walls of the sinuses of the greater part of the pulp tissue are involved. In the true diffuse waxy spleen the

change is confined almost entirely to the pulp tissue, and the Malpighian corpuscles are unaltered or are apparently only somewhat atrophied.

Naked-eye appearances.—The spleen may be very greatly enlarged, much more so than in the sago form. Its substance is firm and elastic, and the margins, like those of the waxy liver, are somewhat rounded. On section, the surface has the peculiar glistening appearance so characteristic of waxy disease in most organs. The edges of the sections are sharp and well defined; the colour is usually a deep red. The trabeculae and Malpighian corpuscles are very indistinctly seen, except in an iodine-stained specimen, where they may frequently be distinguished as yellow points, each of which has a mahogany-brown centre. The yellow points are on all sides surrounded by a mahogany-brown glistening material. It will be noted that the central mahogany-brown point corresponds to the arteriole, the yellow area round it to the adenoid sheath (Malpighian corpuscle), and the mahogany-brown glistening material around this again to the waxy splenic pulp.

Harden (§ 58, 60, or 63) and stain (as in § 348).

($\times 50$).—Examine the methyl-violet stained specimen, and note that most of the Malpighian corpuscles are quite unaffected, and are stained blue, though some of them appear to be somewhat fibroid, the number of cells being then greatly diminished. At some points, however, there is a thin ring of red violet material near the central arteriole, in which position the adenoid tissue is most fully developed. The pulp tissue is markedly affected. The walls of the sinuses are in an advanced stage of waxy degeneration, are stained red violet, and are homogeneous and glistening. Within the sinuses the endothelial cells may be seen as small blue granules near the walls, the red blood corpuscles and leucocytes lying free in the spaces.

($\times 300$).—The central artery of the Malpighian corpuscle is frequently, though not invariably, undergoing waxy degeneration. Around the affected arteriole the small vessels in the sheath may be waxy, but the process seldom extends beyond the immediate neighbourhood of the central vessel. The remainder of the Malpighian corpuscle is fibroid, and may be considerably atrophied, in which case the lymphoid cells are particularly scanty. At the margins of these Malpighian corpuscles the waxy change begins at

once. It appears to take the form of swelling of the fibres of those trabeculae which are in immediate contact with the endothelial cells lining the pulp sinuses. Around the venous sinuses the bands of yellow elastic fibre (the fibres resembling barrel hoops) are seen on section to be considerably swollen and undergoing the waxy change. The rounded cells situated between the sinuses are atrophied, or

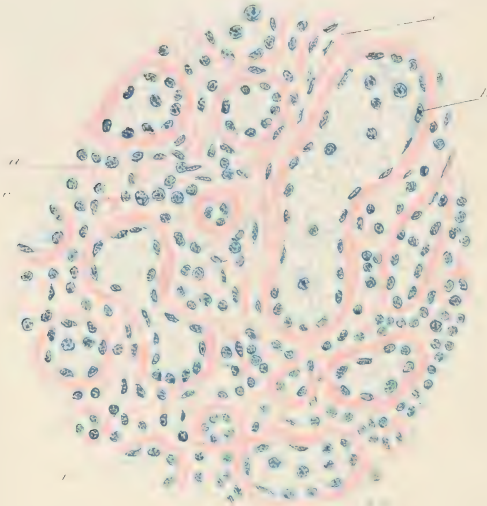


FIG. 168.—Drawing of diffuse waxy spleen, in which the waxy splenic pulp is well seen. Stained with methyl-violet. ($\times 300$.)

- a.* Waxy fibrils.
- b.* Venous sinuses lined with unaltered endothelial cells.
- c.* Small vessel with waxy basement membranes.
- d.* Arterial sinus with waxy basement membrane and unaltered endothelial lining.

fatty and granular, though some appear to be swollen and waxy. It is extremely difficult to give an explanation of this latter appearance, and it is just possible that the waxy, cell-like masses may be sections of some of the swollen fibrous bands. Examine the endothelial cells, many of which are in immediate contact with the swollen sinus walls. These cells do not take on the waxy stain with methyl-violet, but give a blue reaction. Nevertheless, they are sometimes

extremely granular and fatty; this is more readily brought out on the addition of osmic acid (§ 135). In other cases the cells are greatly atrophied, and are detached from the walls of the sinuses, most of which are distended with blood corpuscles, both coloured and colourless.

LEUCOCYTHÆMIA OF THE SPLEEN

350. In the spleen in leucocythæmia we have a great accumulation of leucocytes in, and sometimes around, the pulp sinuses; the spleen is usually enormously enlarged, and may weigh as many pounds as normally it weighs ounces. The enlargement takes place in all directions, so that the organ retains its relative proportions, and the notches on the anterior border remain strongly marked. The organ is firm, pale, and tough, but not leathery. Under the capsule, which is often irregularly thickened, there are sometimes purple patches—small hæmorrhages. These stand out very prominently from the surrounding tissue.

On section the tissue presents a solid homogeneous appearance. The pulp is firm, and of a peculiar grey colour, with small hæmorrhages scattered irregularly through it, but especially near the capsule. Scattered over the surface are cream grey nodules and lines, which represent the Malpighian corpuscles. Embolic infarcts, of very various sizes and in different stages of degeneration (§ 337), may also be observed as yellow wedge-shaped masses situated near the surface.

Examine a scraping from the cut surface ($\times 300$), and note that it contains numerous leucocytes (§§ 208 *et seq.* and 249), a number of coloured blood corpuscles, and some larger cells, composed of a mass of protoplasm, in which are embedded nuclei, sometimes a single one, sometimes several.

Harden (§ 60, 62, or 63), stain (§§ 102, 103, and 110 (*b*)), and mount (§ 195 or 199).

($\times 50$). Note, first, that although the trabeculæ are considerably thickened and the Malpighian corpuscles may be slightly enlarged, they do not form very prominent features in the section. The splenic pulp in the logwood-stained section appears to consist of one mass of deeply stained cells, some of which are much larger than the leucocytes, or even than the normal mononuclear and polymorpho-nuclear endothelial cells. The Malpighian corpuscles may

contain more lymphoid cells, but in some cases they are more fibroid. In certain cases the lymphoid cells of the pulp proper are very few in number.

($\times 300$).—Note the above changes in the Malpighian body and in the trabeculae, both of which may be somewhat hypertrophied. In the former the condition varies slightly in different cases. There is frequently an increase in the number of small round lymphoid

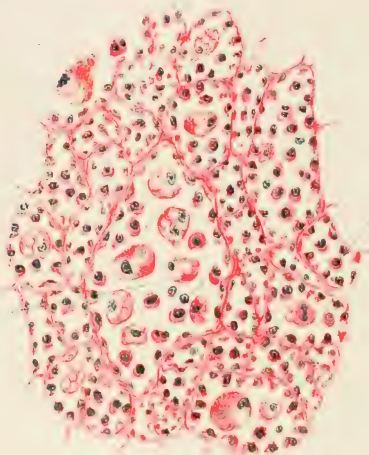


FIG. 169.—Drawing of leucocythæmic spleen. Stained with alum hæmatein and van Gieson's stain. ($\times 250$.)

v.s. Large venous sinus lined with a regular layer of endothelial cells, and containing leucocytes (*l.*) and large cells with one or two nuclei each (*c.*).

e.c. Endothelial plates lining the walls of one of the smaller or arterial sinuses.

cells, together with an increase in the number of endothelioid cells, in which case there is, in this position, a marked increase in the amount of fibrous tissue. These changes are never so well marked as in lymphadenoma, the condition which will next be considered.

In the pulp tissue the most striking feature is the enormous distension of the sinuses. The endothelial cells lining them are swollen and multinucleated, and project somewhat from the walls. To them a number of large cells are attached by a pedicle; these,

like those lying free in the sinus, being probably derived by proliferation from the attached endothelial cells. In these cells there may be only a single nucleus, but very frequently there are several. They usually contain a quantity of altered blood pigment, which is confined principally to these positions, though in some few cases the golden-brown pigment granules may be seen lying in the trabeculæ. In addition to these large cells the sinuses usually contain a number of ordinary leucocytes. In the lungs, in the intestine, and on serous surfaces embolic hæmorrhages are usually very numerous in this disease, as are also fatty degenerative changes in the various organs. For long, lymphadenoma, or Hodgkin's disease, was classed as a form of leucocythæmia, but the changes observed in the two conditions are essentially different. In leucocythæmia the splenic pulp is the part affected, the sinuses being distended with cells (*a*, myelogenous form) of the granular, polymorpho-nuclear type, or (*b*, lymphatic form) of the hyaline and lymphocyte type; whilst in lymphadenoma it is, primarily, the adenoid sheath of the vessels, whence the affection spreads into the surrounding tissue until a considerable part of the pulp may be involved.

LYMPHADENOMA OF THE SPLEEN

351. In lymphadenoma (Hodgkin's disease) there is great enlargement and induration of the lymphatic glands, but there is no great increase in the number of white corpuscles found in the blood.

Naked-eye appearances.—The spleen is usually enlarged, seldom to the same extent as in leucocythæmia, though in some cases it is stated to have weighed from 50 to 80 oz. (1400 to 2250 grms.) or even more.

As in leucocythæmia, the increase in size takes place symmetrically; the notches on the anterior border remain well marked; the outer surface is dark in colour, and over the dark surface there are frequently numerous darker purple spots; the tissue is firm and tough, and in many cases feels quite fleshy, or even fibrous.

On section, the appearance is very characteristic. The general surface has a deep red colour, but scattered over it are numerous small, angular, translucent, yellow masses, almost like small pieces of suet. Some of these are rounded, others are elongated and branching. There may also be large tumour-like masses of adenoid tissue. These,

like the first mentioned, are altered adenoid sheaths or Malpighian corpuscles.

Harden (§ 60 or 63), mount a section unstained (§ 195), and stain one (§ 102 or 103).

($\times 50$).—All the fibrous trabeculæ are increased in size and

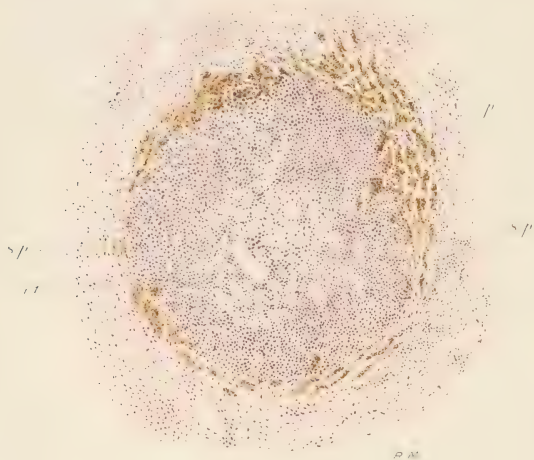


FIG. 170.—Drawing of thickened adenoid sheath in lymphadenoma of the spleen. Section stained with picro-carmin. ($\times 60$.)

f.t. Fibrous Malpighian corpuscle.

p. Pigment near the margin of a Malpighian corpuscle.

s.p. Pulp tissue of spleen encroached upon by growth of fibrous tissue.

thickness. They take on the pink stain very readily, and evidently contain more fibrous tissue than normal.

The Malpighian corpuscles appear to participate in this fibrous change. They are much enlarged, are firm and fibrous, and the lymphoid cells are comparatively few in number. A few larger cells, some containing several nuclei, may be seen arranged in rows between the bundles of fibrous tissue. These (better seen $\times 300$) are not lymphoid cells, but are either endothelioid plates or fibroblasts. At

the margin of the fibroid Malpighian corpuscle there is usually a large deposit of golden-brown pigment, very characteristic of this disease. The pulp tissue is considerably altered, and looks much more solid than usual, especially near the fibroid masses. Away from these the

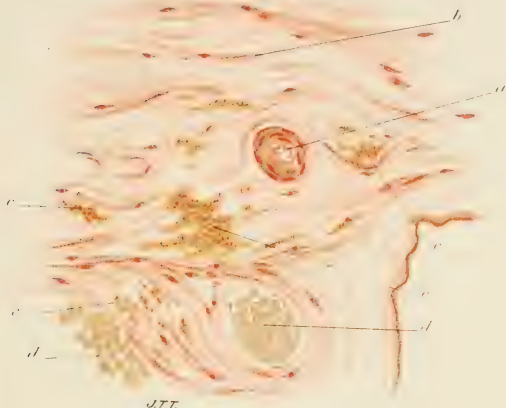


FIG. 171.—Drawing of section of lymphadenomatous spleen.
Stained with picro-carmin. ($\times 250$.)

The drawing is taken from the margin of one of the fibroid
Malpighian corpuscles.

- a.* Small arteriole with walls considerably thickened.
- b.* Well-formed fibrous tissue.
- c.* Pigmented masses—derived from endothelial and other cells containing coloured blood corpuscles in various stages of alteration.
- d.* Cells contained within sinuses, in process of being cut off by the encroaching fibrous growth.

trabecule of the pulp are thicker, the endothelial cells are larger, and frequently contain granules of altered blood pigment.

($\times 300$.)—Note the fibroid Malpighian corpuscles. The lymphoid cells are few in number, and appear atrophied and angular. The spaces between the bands of fibrous tissue are very small indeed, but in them are multinucleated endothelioid cells, which are evidently the

cells by which the large mass of fibrillated periplast is formed. The pigment is usually contained in well-defined spaces (pulp sinuses), and is derived from altered blood corpuscles. Fig. 171 illustrates the process by which it comes to be situated in the fibrous mass. The fibrous tissue grows in all directions around the adenoid sheath, and processes are sent out between the sinuses, which, with their contained blood corpuscles and endothelial cells, are gradually surrounded. The contained blood corpuscles are disintegrated, probably by the endothelial cells, and the blood pigment is set free. The various transition stages are not well represented in the drawing. In the pulp the thickening of the trabeculæ and the proliferation of the large endothelioid cells are easily distinguished; but there is no cramming of the pulp sinuses with leucocytes, as there is in leucocythæmia.

TUBERCLE OF THE SPLEEN

352. Tubercle is seldom or never found in the spleen as a primary growth. It occurs in two forms, (1) miliary tubercle, and (2) larger caseous masses.

(1) The first form is met with in acute general tuberculosis as minute grey, gelatinous, prominent, shot-like bodies in the capsule of the spleen, or near the surface of the organ; a minute yellowish point in the centre of this small mass usually indicates the commencement of caseation. It is a local manifestation of a general disease, and hence is of comparatively little importance.

Harden (§ 60, 62, or 63), stain (§§ 103, 104, or 110 (*b*) and 132), and mount (§§ 193 and 199).

The microscopic appearances are much the same as in miliary tuberculosis of the liver, but it should be noted that here there is usually well-marked congestion of the organ.

(2) The second and more chronic form is the more typical, especially in children. The spleen may be either enlarged or diminished in size. On section, the pulp is usually red and congested, whilst scattered over the surface are bodies which can scarcely be distinguished from the suet like masses seen in lymphadenoma; as a rule, however, they are yellower and more caseous looking, are undergoing softening in the centre, and are about the size of a small pea. The organ in this condition is, like the lymphadenomatous spleen, frequently spoken of as a "hardbake" spleen.

Prepare as above, and note that the appearances are simply those of caseous, or, in rare cases, fibroid tubercle (§ 337).

353. Other growths mentioned as occurring in this organ are *secondary cancers* and *sarcomas*, *syphilitic gummata*, *hydatid cysts*, *dermoid cysts* (very rarely), *simple serous* or *mucons cysts*. A case of *Pentastoma denticulatum* within a calcified cyst has been recorded.

CHAPTER X

THE ALIMENTARY CANAL

354. In the examination of the first part of the alimentary tract for pathological changes, it should be remembered that the epithelium in the oral cavity, in the lower part of the pharynx, and in the œsophagus, is of the pavement or stratified type, which differs only from that on the cutaneous surface in the fact that it is more delicate and is covered by little or no horny layer. In the upper part of the pharynx, however, the epithelium is columnar and ciliated, and extends down into the folds of, or depressions in, the mucosa. The mucosa varies somewhat in thickness in different parts of the tract, but throughout it has the same structure. It consists of dense connective tissue, from which are upward prolongations, forming papillæ, on which the deeper cells of the epithelial layer rest. It is intersected or channelled by a dense network of lymphatics and lymph spaces. The mucosa is continued into the submucosa (except in the œsophagus, where it is separated by a few delicate bundles of non-striped muscle cells), which is composed of a looser and more lamellar connective tissue, and "contains masses of fat cells, the large branches of vessels and nerves, the glands, and striped muscle, and, extending outwards, forms a continuity with the connective tissue of the surrounding organs as muscle, periosteum, skin, etc." (Klein and Noble Smith). The large mucous glands, embedded in this submucosa, are identical in structure (compound tubular glands) throughout, varying only in number and size in the different regions of the first part of the tract; they are largest and most numerous in the mouth, and least numerous in the œsophagus.

As on the cutaneous surface, these structures are affected, in inflammation, according to the intensity of the process; there may be simply a transient redness, or there may be such marked vascular and interstitial changes that removal of epithelium or sloughing of the deeper tissues may ensue.

"FUR" TAKEN FROM THE TONGUE

355. Even in health the "flora" of the mouth is a very luxuriant one; under certain conditions it becomes still more rich. Almost all the micro organisms usually found in air and water may, at some time or other, be found in this position. In decaying teeth and in the tartar

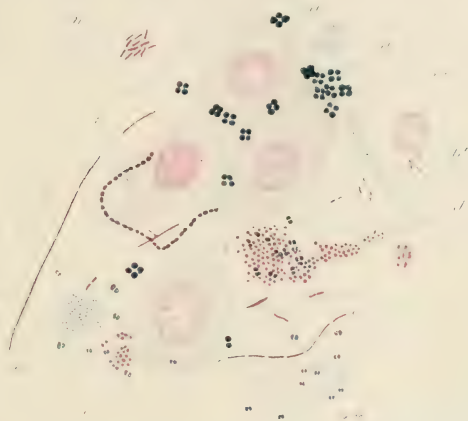


FIG. 172.—Microscopic preparation of the "fur" taken from the tongue of a child suffering from scarlet fever, fifth day of the disease. Stained by Leishman's method. ($\times 1000$.)

- a. Large epithelial scales.
- b, b'. Long unjointed leptothrix or thread-like bacteria.
- c. Jointed leptothrix.
- d, d'. Staphylococci.
- e. Diplococci.
- f. Streptococci.
- g. Micrococcus tetragonus.
- h. Spirilla.

Various other organisms are seen, some with terminal spores (h.).

growing on them, in the sordes on the gums, and in the fur on the tongue, bacteria, yeasts, etc., of great variety and in enormous numbers may be found.

The fur taken from the tongue of a scarlatinal patient during the first week of the fever affords a good example of this. Stain (§ 153), $\times 1000$. Note first the large epithelial scales derived from the buccal mucous membrane, then the sarcina or micrococcus tetragonus, the

various rod-shaped and spiral organisms, some short, others developing into long filaments, some segmented, others without any division. Diplococci, single or in chains, are fairly numerous; staphylococci and streptococci, the former of different sizes, may also be seen.

APHTHOUS PATCHES

356. The aphthous patches which occur during the course of teething and a variety of inflammatory diseases are most frequently met with on the inner surface of the lips, and on the gums, tongue, and soft palate in children.

Naked-eye appearances.—The patches vary in size from that of a pin-head to that of a small wafer, and are white or yellowish-grey, dull and opaque; the mucous membrane around them is injected, red, or sometimes purple, and has a peculiar glistening, semi-transparent appearance. Several of the smaller patches may coalesce to form larger ones.

The peculiarity in this condition is, that although the white patches may be separated from the subjacent tissues, the separation is seldom followed by any well-marked ulceration. The reason of this will be apparent when the microscopic examination is made.

Harden (§ 60), cut sections at right angles to the surface, stain (§§ 102, 103, and 110 (*b*)), and mount (§§ 195 or 193 and 199).

($\times 50$).—The changes are almost entirely confined to the epithelial layer. There is undoubtedly congestion of the small vessels of the mucosa, accompanied by a migration of leucocytes, some swelling of the connective tissue, and even infiltration of the spaces between the superficial layers of connective tissue fibrils with fibrin; but the most prominent changes are swelling of the epithelial cells, exudation of fibrinous lymph and emigration of polymorpho-nuclear leucocytes, first between the epithelial layer and the mucosa, and then between the individual epithelial cells. The swollen epithelial cells, with the fibrinous exudation beneath and around them, form the opaque aphthous patch; the epithelium is regenerated very rapidly.

($\times 300$).—Note the slight swelling of the connective tissue of the mucosa and the increased number of leucocytes around the distended vessels. In the patch the fibrinous lymph, in which, often, are numerous polymorpho-nuclear leucocytes beneath and between the swollen epithelial cells, is considerably increased in amount.

There are changes in the epithelial cells, beyond the mere increase in size; some of them are vacuolated, the nucleus then being placed at one side of the vacuole, whilst others, especially those in the immediate neighbourhood of the patch, are undergoing rapid proliferation, as is evidenced by the large number of cells in which two nuclei are seen, or in which division of the nucleus has begun.

In these aphthous patches long branching strings of ovoid or lanceolate bipolar staining almost yeast-like organisms may be seen separating the buccal epithelial cells. Stain (§ 173, counterstaining

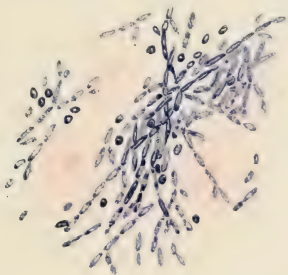


FIG. 173.—Cover-glass preparation of a fragment of the membrane from the mouth of a child suffering from “thrush.” The buccal epithelial scales stained red, and the thrush fungus—*Oidium albicans*—stained violet, especially at the poles of the individual organisms. Specimen stained with gentian-violet and safranin. ($\times 400$.)

with safranin) and examine ($\times 400$), when the above features may easily be distinguished.

MUCOUS PATCHES

357. Mucous patches, due to infiltration and proliferation of the epidermis and the underlying tissue, are met with in cases of syphilis, and may be taken as fairly representative of a more extensive inflammatory process. They are usually found at the angles of the mouth, on the tips and side of the tongue, and frequently on the tonsils; but they may be seen on almost any part of the mouth, or near any of the orifices of the body where the skin is kept moist and in folds.

Naked-eye appearances.—They are small, flattened, opaque, white

patches, with a peculiar, moist, silvery grey or glistening surface. On passing the finger over one, it is found to be slightly indurated, or, if of long standing, the induration is well marked, and the thickening very distinct. The formation of the patch may be followed by ulceration, beginning at the centre (in the tonsil this, according to Cornil and Ranvier, is comparatively rare).

Harden and stain as for the aphthous patch (§ 356).

($\times 50$).—The appearances presented are somewhat similar to those seen in the aphthous patch, but the changes are more extensive. Near the margin, the horny epithelial layer extends for some distance only over the patch, and even where it is present the squames are swollen and are separated by leucocytes and small masses of fibrin. Nearer the centre there is enormous swelling of the polygonal cells of the rete Malpighii; some of these are breaking down rapidly; whilst around these cells, or infiltrating the spaces between them, is coagulated fibrin, stained red with eosin, and polymorpho-nuclear leucocytes, the nuclei of which are stained violet with logwood. Near the surface the fibrin appears to predominate, whilst in the deeper layers the leucocytes are in excess. At the margins of the patch, and near the mucosa, the epithelium is proliferating rapidly, giving rise to part of the thickening seen with the naked eye. In the mucosa, and in some cases even in the submucosa, the distension of the vessels is well marked. Around the vessels the accumulation of small round cells may be very great; there is also considerable swelling of the connective tissue, and at the same time an accumulation of fibrinous lymph between the swollen fibres, in the lymphatic vessels and lymph spaces. This affection of the deeper tissues is here extremely well marked, and in this respect the mucous patch differs from the aphthous patch.

($\times 300$).—Confirm the above appearances.

Stain (§ 158). ($\times 1000$).—Confirm the above and examine for spirochaetes (§§ 243 and 493).

DIPHThERIA OF THE PHARYNX OR LARYNX

358. In diphtheria there is exudation of a false membrane on to the mucous membrane of the upper part of the larynx, pharynx, palatal arches, tonsils, and especially on the posterior surface of the soft palate or uvula. The last named is one of the best positions in which to examine the changes induced. The appearances vary according to the date of the disease at which the patient succumbs. If there are simply

swollen greyish patches scattered over a dull red background, the



FIG. 174. —Fibrinous lymph, so-called false membrane, on the surface of the larynx. Stained by Gram's method. ($\times 50$.)

- a.* Surface of fibrin on which are a number of diphtheria bacilli and other micro-organisms, especially micrococci.
- b.* Groups (pure culture) of diphtheria bacilli, below the surface.
- c.* Open network of coagulated fibrin in which are a few leucocytes.
- d.* Denser network of fibrin pushing its way into the superficial lymphatics. The remains of epithelial cells may be made out. Coagulation necrosis.
- e.* Layer of leucocytes and proliferating cells.
- f.* Dilated blood vessel filled with red blood corpuscles.
- g.* Groups of leucocytes and proliferating cells.
- h.* Glandular structure of trachea.

epithelium is usually still present, though very much altered ; if a definite

washleather-like membrane is present, the whole arrangement of tissues is altered.

If this membrane be detached from the larynx or trachea there may be little bleeding, the membrane bringing away with it simply the columnar epithelium and leaving a surface from which, as a rule, no hæmorrhage takes place. The membrane appears to be much more firmly and deeply attached to the uvula or pharynx, and bleeding follows any attempt to separate it from the tissues below.

Harden a piece of the uvula or a section of the larynx with the membrane on its posterior surface (§ 58), stain (§ 117), and mount (§§ 193 and 199).

($\times 50$).—In the Gram-stained section of the larynx the congested mucosa immediately beneath the basement membrane is well seen. There is a slight increase in the number of leucocytes in this position, especially around the smaller congested vessels. Above the mucosa is a layer of coagulated fibrin in which are a number of spaces, the whole forming a kind of network. Embedded in this fibrin are a number of leucocytes in various stages of degeneration. On the surface of the membrane are small collections of deeply stained organisms. In the section from the uvula or pharynx it will be seen that the coagulated fibrin has accumulated in the lymph spaces, especially in those of the adventitia of the smaller vessels. It has made its way between the squamous epithelial cells, carrying some of them away with it, so that they are embedded in a mass of coagulated fibrin. The fibrin is arranged in a coarse network, some of the spaces in which are filled with epithelial cells in various stages of alteration. Rounded or oval masses of bacilli may be seen in this coagulum, most of them near the free surface, but some of them deeper down.

($\times 300$).—On the surface of the false membrane, and extending for some distance into the tissues, are masses of micro-organisms which take on the methyl-violet staining very deeply. The epithelium forms merely a heavy network, of which the margins of the cells with the coagulated fibrin deposited between them form the meshes. The body of the cell has undergone first coagulation necrosis and then a regular liquefaction, after which it disappears, leaving the network above described. Beneath this altered epithelial layer the connective tissue is infiltrated with fibrin and leucocytes, most of which are accumulated around the distended blood vessels. Around the distended vessels hæmorrhages are frequently seen, but there are as yet few bacilli

in the lymphatics and in the deeper tissues generally, and the cell infiltration is confined to the tissues immediately beneath the epithelium at the point of infection.

At a later stage, when the false membrane has formed, and perhaps has sloughed away, leaving a grey, sodden, sloughy, and infiltrated-looking surface, examine a piece of the tissue prepared as above.

($\times 450$).—The connective tissue of the mucosa is transformed into a mass of fatty, degenerated, or homogeneous material, which is very characteristic of the diphtheritic condition. A fibrinous exudation, in which the masses of bacilli and micrococci are situated, make up the false membrane on the surface. The blood vessels in the deeper tissues are distended, and are surrounded by a number of round cells or leucocytes. This accumulation of cells takes place especially at the point of junction between the mucosa and the deeper tissues. The lymphatics for some distance round are choked with fibrin in which are embedded a few leucocytes; in cases where the patient succumbs rapidly they are filled with masses of bacilli and micrococci, which also may be found in any part of the slough.

The grey sloughy part is usually teeming with masses of deeply stained micrococci, but there is now no trace of epithelial structure left. In addition to micrococci, occurring almost invariably in the early stages in cases of true diphtheria, are groups of thin curved rods, never rigidly straight, 3 to 6 μ in length, and 0.3 μ in breadth, with ends sometimes pointed, sometimes rounded and thickened. ($\times 1000$ to bring out details.) They stain deeply with methylene-blue, rarely uniformly; often they have a striped or beaded appearance, small glistening points appearing in their substance. These have been described as spores, but they consist merely of altered protoplasm. In some of the bacilli there is a distinct metachromatic reaction with methylene-blue, the swellings and granules taking on a deep violet tint. Where the disease is more advanced, the rods become pear-shaped and club-shaped bacilli. In a few cases the swelling at one end is so distinct that the organism is compared to an Indian club in shape—in this case the banding is often exceedingly well marked; the bacilli in some cases are much shorter, in others again considerably longer than those mentioned, the shorter forms are usually rounded and stained at the extremities with a lighter band between; in some cases, however, they are like double cones with the bases opposed. In some very old membranes it is difficult or impossible to distinguish any

characteristic rod-shaped bacilli, the micrococci and other micro-organisms becoming more numerous, especially as the surface becomes foetid and softened. In such cases the rod-shaped bacilli can only be found entangled in the deeper network.

The distinctive characteristics of this condition as compared with so-called croup are—that in diphtheria the specific micro organisms, the slough, and a toxic condition are almost invariably present, but the marked fibrinous exudation, though usually present, is not essential; whilst in croup the exudation is essential, and any micro-organisms that may be present are found only on the surface; no toxic symptoms are produced; of such micro-organisms in croup the “specific” Klebs-Loeffler bacillus is said never to be one.

DIAGNOSIS OF DIPHTHERIA DURING LIFE

359. In the diagnosis of diphtheria during life, the following methods of staining and cultivation are employed. Remove a portion of the membrane from the patient; to do this tie a piece of cotton wool firmly to a pair of forceps or to a penholder, and with this rub the surface of one of the grey patches, or detach a small fragment of the membrane. Remove this with a bit of blotting paper and place it between two cover-glasses, where it is broken down as finely as possible; the cover-glasses are then separated and heated over a flame in the ordinary fashion (§ 182), and stained with Loeffler’s methylene-blue (§ 115) and by Neisser’s method (§ 186).

Stain another fragment of the membrane, freshly teased out, with picro-carmin (§ 102), and mount (§ 195).

Loeffler makes diagnostic cultures as follows: with a platinum needle beaten out at the end to form a kind of spatula, he detaches a particle of the false membrane (it should have been noted that the diphtheria bacilli are always present in greatest numbers in the older or more superficial portion of the membrane—consequently they may usually be removed by a “swab” or a spatula); he then makes stroke cultures on the surface of blood serum prepared according to the following formula :—

Blood serum	3 parts.
Neutral peptone broth (1 per cent. grape sugar)	1 part.

This is sterilised in the test-tube at a low temperature (57° C.), applied for one hour a day on eight successive days, the medium being allowed to remain at the ordinary room temperature in the intervals. It is then solidified in a slanting position by heat.

The same "charged" needle is used without being recharged to inoculate some half dozen tubes. In place of this spatula a "swab" or pledget of absorbent cotton wool wrapped round the end of a piece of iron wire, sterilised in a test-tube, may be used. The pledget is rubbed over the membrane and then over the surface of the serum medium. When these are incubated at from 33° to 35° C., colonies of bacilli are visible at the end of twelve or sixteen hours, and within twenty-four

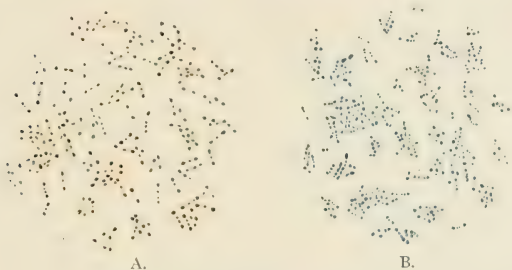


FIG. 175.—Diphtheria bacilli taken from a twelve hours' blood serum culture. ($\times 1000$.)

A. Stained by Neisser's method.

B. Stained with methylene-blue.

Note differential staining bringing out "beading" very distinctly in both cases

hours they appear as small rounded greyish-white points, the centre of each of which is more opaque than the periphery, they spread rapidly, form greyish rounded discs, and continue to develop so quickly that they are usually well formed before the other organisms have begun to form a colony at all visible to the naked eye. The bacilli have all the characters already described, and when seen in specimens made from cultivations are arranged very irregularly in groups. They have been compared to Chinese letters or to "spillikins": this is rather an important feature, as certain other organisms which resemble them in appearance may be distinguished from them by their somewhat regular arrangement.¹

¹ For fuller particulars as to method of diagnosis, the student is referred to Muir and Ritchie's "Manual of Bacteriology."

THE STOMACH

360. Normal histology.—The wall of the stomach, like that of the œsophagus, is composed of mucous, submucous, muscular, and peritoneal coats. Here, as in the small and large intestine, the secreting glands are confined to the mucosa, the epithelium covering this layer and lining the various gland ducts of the stomach is distinctly columnar; it rests upon a basement membrane composed of flattened endothelioid cells. At the cardiac end the simple peptic glands are straight or slightly curved tubular glands lined with chief or central columnar epithelial cells with circular nuclei, with large or angular oxyntic cells with ovoid nuclei outside these chief cells. Near the neck of the gland these oxyntic cells are very numerous and abut on the lumen of the duct. At the pyloric end the glands are larger and more complicated, each dividing into several sinuous and convoluted tubes; they are lined with the regular columnar cells, and have none of the large spherical or angular cells near the basement membrane. Supporting the gland tubes is a delicate mucosa similar to that described in the œsophagus, and beneath or in this is a *muscularis mucosæ* separating it from the submucosa. The submucous tissue consists of a delicate supporting connective tissue resting upon the non-striped muscular wall of the stomach, which has both inner, circular, and outer longitudinal layers. Covering the stomach is a fold of peritoneum, which is similar in structure to that covering the organs already described,—the liver for example. A most interesting fact in connection with the vascular supply of the walls of the stomach is put prominently forward by Cornil and Ranvier,¹ who state that the arteries which supply the mucous membrane “all enter by the peritoneal surface, and ramify in the successive layers of the stomach, so that the zone of distribution of each arteriole in the mucous layer forms a cone, the apex of which reaches the submucous tissue, and the base the surface of the mucous membrane of the stomach.”

INFLAMMATION OF THE MUCOUS MEMBRANE

361. The stomach is one of the least satisfactory organs with which the pathologist has to deal. In it post-mortem changes take place so

¹ “Manual of Pathological Histology.” English translation by A. M. Hart, vol. ii. pt. i.

rapidly that any pathological processes of recent date are at once masked, and even those of longer standing are considerably altered. It is, therefore, impossible to give an exact and non-arbitrary account of either the naked-eye or microscopic appearances presented in diseased conditions.

In acute inflammations of the stomach—in acute catarrhal gastritis, for instance—it is an extremely difficult matter to determine how far the appearances presented are induced by the inflammatory condition, and how far they are due to post-mortem changes. Even in a healthy stomach, the epithelium has almost entirely disappeared, being digested by the gastric juice, by the time a post-mortem examination can be made, so that in acute gastritis, beyond the changes usually taking place in acute inflammations, little is to be observed. As one would expect, however, the secretion of mucus is greatly increased, and the swollen and dark red mucous membrane is covered with a layer of mucus, with, here and there, small extravasations of blood.

($\times 300$).—Distension of the blood vessel, often accompanied by small hæmorrhages, extravasation of leucocytes, and swelling and proliferation of the endothelial cells of the lymphatics, are the most noticeable features, epithelial changes as a rule being indistinguishable for the reason above given; but, where they can be made out, the epithelial cells contain large globules of mucin and are desquamating or undergoing disintegrative changes, whilst the epithelial cells of the peptic glands are usually granular, often detached.

Chronic changes, where there is an atrophied condition of some structures, or where there is new formation of fibro-cellular tissue, are more readily identified.

“COMMON,” “CHRONIC,” “CIRCULAR,” “PERFORATING,” OR
“SIMPLE” ULCER OF THE STOMACH

362. This ulcer is usually single, though from two to four may occur simultaneously. It is situated, in most cases, on the posterior wall, or on the lesser curvature near the pyloric end of the stomach (sometimes a similar ulcer is found in the duodenum); it measures from one-half to two-thirds of an inch in diameter (1.25 to 1.6 cm.).

The *naked-eye appearances* are very characteristic. The edges are seldom much injected or raised from the surrounding tissue, the margins are quite vertical, and the floor is smooth, pale dry, and

fibrous. It is rounded or oval in shape and it looks as if it might



FIG. 176.—Section of perforating gastric ulcer. Stained with logwood and eosin. ($\times 15$.)

- a.* Mucous membrane, with slightly increased cellular intertubular tissue which has fallen over the edge of the ulcer.
- b.* Submucosa.
- c.* Submucosa in a state of necrosis.
- d.* Muscular coat in a state of necrosis.
- e.* Layer beneath necrotic tissue. Here slight cell proliferation or migration is seen.
- f.* Normal muscular coat, increased number of cells in septa.
- g.* Normal muscular coat.
- h.* Subperitoneal coat somewhat thickened—inflammation.
- i.* Peritoneal coat with layer of fibrinous lymph on the surface.

have been punched out with a wad-punch. The depth varies greatly

in different cases. In some instances the mucous membrane only is involved. The punched-out appearance in such cases is very well marked. If the ulcer extends more deeply so as to eat through the muscular coat, there is a peculiar terraced appearance, as though a smaller punch had been used for the deeper layer, and a somewhat funnel-shaped opening, corresponding in shape to the conical distribution of the artery already mentioned, is the result. In some cases the acute ulcerative process has ceased, but the ulcer has not healed, and slight thickening of the surrounding tissue has ensued. When these ulcers perforate, it may be only by an exceedingly small hole, they may open into the pancreas, liver, or spleen; or into the peritoneal cavity,—when abscesses or peritonitis usually result,—or into some of the surrounding blood vessels, such as the coronary arteries of the stomach or the large splenic vessels. Adhesions and fistulous openings into the duodenum, transverse colon, or the pleural or pericardial sacs may also be met with. Even after perforation, the ulcers may heal, and healing may take place so perfectly that, except on very careful examination, no scar can be distinguished. This is especially the case where, though the ulceration has been acute, the destructive process has not been extensive. Where the loss of tissue has been great, the contraction of the new cicatricial tissue formed during the process of healing gives rise to a puckered or stellate scar. It is generally agreed that the cause of the solution of continuity is the cutting off of the blood supply from a definite area, which, deprived of its nutrition, is acted upon by the gastric fluids and softened. That the process is acute is also agreed, but there is some difference of opinion as to the cause of obstruction to the flow of blood. Spasm of the vessels, atheroma and thrombosis and embolism—each has its advocates; but it appears probable that any of these may be the cause of the cutting off of the blood supply, and that the digestive action is then allowed to go on in the devitalised patch of tissue originally supplied by the obstructed vessel.

Several cicatrices may occur running into one another, especially in the middle zone of the stomach, when by their contraction they give rise to what is known as the hour-glass stomach.

Harden such a thickened ulcer (§§ 58*a* and 60 or 63), stain (§§ 102 or 104, and 110 (*b*) and 132), and mount (§ 195 or 199).

($\times 15$).—The funnel shape of the ulcer is well seen, though there is evidently a greater loss of tissue in the submucosa than in the mucosa proper which falls in over the margin of the ulcer. The ulcer,

as it involves the muscular tissue, is distinctly funnel-shaped ; in this case the muscular coat has been completely perforated. The subperitoneal tissue, though somewhat thickened beneath the ulcer, is evidently invaded. On the peritoneal surface is a layer of coagulated lymph, the result of an inflammatory process. The floor of the ulcer now consists of a layer of coagulated fibrin, in and beneath which are a number of leucocytes, though this is all the further evidence we have of any inflammatory process. In the submucosa and even between the bundles of the muscular coat there is a slight increase in the number of small nucleated cells ; the same holding good for the subperitoneal tissue. In this instance one can follow the line of the necrosis quite distinctly. When the circulation through the inverted cone of vessels is obstructed (in any way) and the nutrition cut off from the tissues supplied, these tissues are digested and removed and an ulcer results. At first there is little or no evidence of any inflammatory change. Later we have some cellular infiltration, as seen above. The layer of fibrin and granulation tissue on the surface of the ulcer is always thin, as the gastric juice soon acts upon any tissues that are not fully supplied with blood and lymph. The point at which perforation would take place is easily made out. The thickened subperitoneal tissue may stave off this perforation for some time, and even altogether until healing takes place.

($\times 50$ and $\times 300$).—Around the ulcer, in its immediate neighbourhood, there is slight increase in the number of small deeply stained cells in the mucosa, in the submucosa, and between the bundles of muscle fibres in the muscular coat ; the glands are little altered, except that they stand out more prominently than in the normal condition. Further changes, such as thickening of the walls of the vessels near the ulcer and diminution of their calibre ; and where the muscular coat is invaded, fatty degeneration and fraying out of the muscular fibres, are described (Cornil and Ranvier), but are not seen in the specimen under examination.

POST-MORTEM DIGESTION OF THE WALL OF THE STOMACH

363. It has already been noted in describing the gastric ulcer, that when the blood supply is cut off from any part of the wall of the stomach, such part is rapidly digested. It has also been observed that in certain diseases, especially in inflammatory diseases of the brain, and

where the process of digestion is going on vigorously from the large quantity of acid gastric juice present, the whole mucous wall may be partially digested. Far more commonly we find, however, that digestion is continued after death, especially when the stomach "contains an excess of gastric juice, or of acid products of decomposition" (Ziegler). In such cases the colouring matter is dissolved out from the red blood corpuscles, the various coats become softened, and are readily broken down. There is never any thickening or redness of the parts where the softening is taking place, in fact there are no signs of inflammation of any kind. Where perforation has taken place, the margins of the opening are ragged, friable, and pale or dark grey according to the amount of blood in the parts before death occurs. This condition is perhaps best seen in children in whose stomachs much undigested food is found. I have seen it well marked in two cases examined on one day, and in warm weather as many as four out of five cases have given some evidence of this condition.

THE SMALL AND LARGE INTESTINE

364. Normal histology.—In the wall of the small intestine the coats are very like those of the stomach, but one or two differences must be noted. The mucosa is thrown into a series of crescentic folds, which form valve-like projections along the course of the tube. These, the *valvule conniventes*, have essentially the same structure as the rest of the mucosa. Over the whole surface are small rounded finger-like prolongations or villi; in the centre of each of these are large lymph spaces or chyle vessels, surrounded by longitudinal muscular fibres and a loop of capillary blood vessels. Between and at the bases of the villi are simple gland tubes, known as the crypts of Lieberkühn. Extending over the whole mucous surface, covering the villi and lining the crypts, is a layer of columnar epithelium, with here and there a few goblet or mucus-secreting cells. The basement membrane, composed of endothelioid cells, separates the epithelial cells from the connective tissue of the mucosa. The *muscularis mucosæ* is here an important structure, but is similar to that of the stomach, and the submucosa, the internal circular muscular fibres, the external longitudinal fibres, and the peritoneal covering have all their homologues in the stomach. The Brunner's glands (compound racemose glands) are embedded in the submucous tissue of the duodenum, whilst the lymph follicles, in the

form of solitary glands and Peyer's patches, are contained partly in the submucous coat and partly in the mucosa. These glandular masses are simply single masses of adenoid tissue, and collections of the single glands. The solitary glands with the structure of ordinary lymphatic glands, have a trabecular framework and the adenoid tissue proper; they are composed of a delicate fibrillar and membranous reticulum, on the strands of which rest flattened endothelioid cells, and between which are the lymph corpuscles. Covering these masses of adenoid tissue is a layer of cubical epithelial cells.

The Peyer's patches are elliptical, run in the longitudinal axis of the intestine, project slightly above the general surface, and are composed of numerous solitary glands. They are found on the side of the intestine away from the mesenteric attachment, and are most numerous at the lower part of the ileum.

In the large intestine there are no villi and no Peyer's patches, but the solitary glands are larger than in the small intestine.

TYPHOID LESION OF THE INTESTINE, LEADING TO THE FORMATION OF THE TYPHOID ULCER

365. In this condition there is first marked swelling of the elements of the adenoid tissue of the intestine—the solitary glands, and the Peyer's patches. The disease is therefore most marked in those positions where the glands are most numerous—at the lower end of the ileum. It may spread upwards, and, though rarely, downwards; in the earlier stages—during the first week—there is a progressive swelling of the solitary glands, which at first are pink and semi-transparent, soft and pulpy in appearance and to the touch; later they become paler and firmer. All the Peyer's patches at the lower part of the intestine become involved throughout their whole extent, as do also the solitary glands. These patches are sharply raised, “and winding ridges, not unlike the cerebral convolutions in miniature” (Ziegler), appear on their surface, especially where the mucous membrane is swollen and somewhat paler than the surrounding tissue.

Harden (§ 60, 62, or 63), stain (§§ 102 or 103 or 110 (*b*) and 132), and mount (§ 195 or 199).

In the earlier stages the patches are very vascular, and small hæmorrhages may appear on the deeply congested surface. The mucous membrane near the swollen patch, owing to infiltration of the

mucosa, distension of Lieberkühn's follicles, and obliteration of the villi, is smooth. The gland is swollen, and projects into the lumen of the intestine, pushing before it the epithelial layer of the mucous membrane.

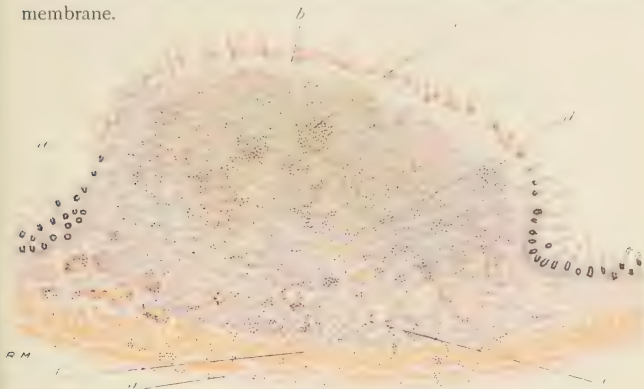


FIG. 177.—Section through a swollen Peyer's patch of the small intestine in an early stage of typhoid fever. Stained with logwood and eosin. ($\times 15$.)

- a. Normal mucosa.
- b. Mucosa, necrosed (badly stained).
- c. Swollen lymphoid tissue of Peyer's patch, tissue badly stained.
Cells numerous and fibrils swollen.
- d. Congested blood vessels.
- e. Comparatively normal tissue beneath, but fibrils swollen.
- f. Muscular tissue.
- g. Subperitoneal and peritoneal tissue.

($\times 400$).—If a small portion of the swollen gland be teased out, a number of much larger multinucleated hyaline cells, derived from the endothelioid cells lying on the retiform tissue of the gland tissue, are brought into view; swollen fibres, lymphocytes, and leucocytes are also seen in large numbers. Short, rod-shaped bacilli, present during this stage of the process, may be seen in scrapings made from the adenoid tissue of the mucous membrane or from the mesenteric glands. To see these bacilli, rinse the fresh scrapings or sections in a 1 per cent. solution of corrosive sublimate, stain with gentian-violet (§ 171, 172, or 173), and mount (§ 195 or 199).

($\times 15$).—The most marked features seen under this power, are (a) the degenerated condition of the epithelium of the glands of the mucosa

—the nuclei of these cells do not take up the nuclear stains; (*b*) the tissue in which these cells are embedded is also badly stained; (*c*) the adenoid tissue beneath is markedly congested, and there is evidently some migration of leucocytes and lymphocytes and proliferation of cells. Even under this power the swelling of the fibrillar network of the adenoid tissue may be made out. In the tissue between the lymphoid mass and the muscular coat the distended blood vessels form a prominent feature. Around or in the neighbourhood of these vessels are accumulations of nucleated cells, many of them apparently leucocytes, and the fibrous tissue is distinctly swollen and homogeneous. Some of the blood vessels running between the bundles of the muscular coat are also congested, but, as a rule, there is little or no change in the subperitoneal and peritoneal layers.

($\times 50$).—Confirm the above.

($\times 300$).—Note that the degenerative changes are confined not merely to the mucosa and submucosa; the swollen fibres of the reticulum of the lymphoid tissue, the proliferating endothelioid cells, the lymphocytes, and even the polymorpho-nuclear leucocytes in this reticulum take on the stain badly, whilst here and there the red blood corpuscles appear to have escaped in considerable numbers from the distended and weakened vessels. Beneath this necrosed or degenerating tissue the swollen fibrous tissue, in which run congested vessels, sometimes surrounded by distinct groups of nucleated cells, many of them polymorpho-nuclear leucocytes, but some of them lymphocytes and mononuclear cells, with here and there a few plasma cells, may be seen. The muscular and peritoneal tissues are little affected except in very severe cases, when the non-striped muscle fibre appears to be swollen and granular; immediately under the swollen patch the fibres may be seen to be “absorbed” or encroached upon by the new cellular tissue.

When the swollen patches have become very tense and pale, the stage of sloughing sets in. The slough usually involves both the mucous and the submucous tissue. It is invariably bile stained, and very frequently blood stained, from rupture of some of the small blood vessels in the muscular coat. It comes away in fragments; but if violence of any kind is used, and the slough is dragged away from the softened tissues beneath, laceration may ensue, and sometimes resultant perforation of the intestine. Notice that, although all the glands and patches are swollen, comparatively few are ulcerated; and even these latter may not slough throughout their whole extent. In the Peyer's

patch, for example, the ulcer may involve the central width of the patch, but may extend for some distance on each side, as one would be led to expect from the infiltration of the neighbouring tissues. On the other hand, the ulcer very frequently has the shape of the Peyer's patch, or

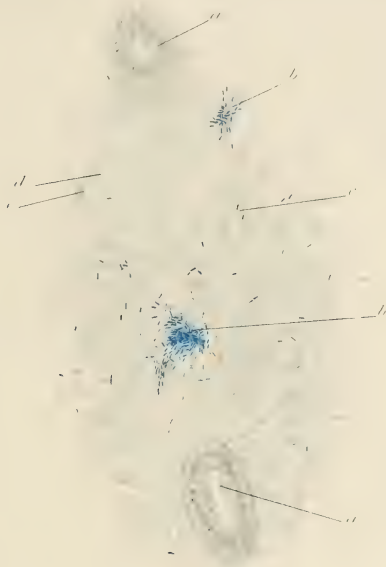


FIG. 178. Section of typhoid ulcer of intestine—ileum. Specially stained with gentian-violet (§ 365). ($\times 450$.)

- a. Gland tubules.
- b. Groups of typhoid bacilli.
- c. Single bacilli. (These are represented rather longer than, and not quite so rounded at the ends as they appeared in the specimen.)
- d. Small lymphoid cells in reticulum.
- e. Large endothelioid cells.

of the solitary gland, as the case may be. Where the whole of the patch is involved, the ulcer is oval, and its long axis corresponds to that of the bowel. The floor, which is usually composed of the circular muscular coat of the intestine and of granulation tissue, is smooth,

injected, and glossy, but there is comparatively little thickening. The margins are ragged, much undermined, and can be readily floated out in water. They are made up of the mucous membrane and submucous tissue, though where the ulceration has extended through the circular muscular coat, the longitudinal fibres may form the floor of the ulcer, and the free ends of the circular fibres may then form part of the overhanging margins. The peritoneum is seldom much thickened, though some infiltration is often met with.

The ulcer may heal without leaving a marked cicatrix, the edges simply falling down and uniting with the floor; there is no new formation of glandular tissue, the epithelium grows over from the margins, and a smooth, greyish, very characteristic patch is left. On the other hand, perforation may result from extension of the ulcerative process; this is usually accompanied by hæmorrhage.

Harden (§§ 57 (*a*) and 58 or 63), stain (§§ 102 or 103, or 110 (*b*) and 132), and mount (§ 195 or 199).

($\times 15$).—In a section of a typhoid ulcer in which only a portion of the Peyer's patch is involved, the swollen necrosed lymphoid tissue with its overlying layer of mucosa is broken down, leaving an ulcer with well-marked features and of characteristic type. There is some cellular infiltration of the tissue between the tubular glands at the margin of the ulcer. In the tissues in the neighbourhood of the ulcer there is marked congestion and great cellular infiltration. On the floor of the ulcer is necrosed tissue, which does not take on any nuclear stain; (this is a bile-stained area, seen with the naked eye) and beneath it are numerous nuclei. The layer of muscle fibre immediately beneath the floor is greatly fragmented, the fibres, granular and irregular, are being absorbed, apparently by the new cells; the subperitoneal muscle fibres are much swollen, and between the bundles and in the subperitoneal tissue is marked evidence of a proliferative change similar to that met with in the lymphoid tissue of the Peyer's patch or solitary gland. Note that in the section figured there is some lateral extension of the necrotic and ulcerative process beneath the mucous membrane; in some cases this burrowing is much more marked than is here represented.

($\times 50$).—Observe the shape of the ulcer, the overhanging margins, with the follicles and papillæ of the mucosa on the upper surface. In all the tissues bounding this ulcer—the overhanging walls, and the smooth muscular floor—there is evidently a considerable amount of swelling of fibrils and of small cell infiltration extending throughout the mucosa,

there giving rise to swelling between the villi, which are partially obliterated.

($\times 450$).—Confirm the above. Note also that in the swollen adenoid tissue, solitary or small groups of bacilli may be seen lying in the lymph spaces, and sometimes, though rarely, in the substance of the large endothelioid cells. The fragmented and granular appearance of

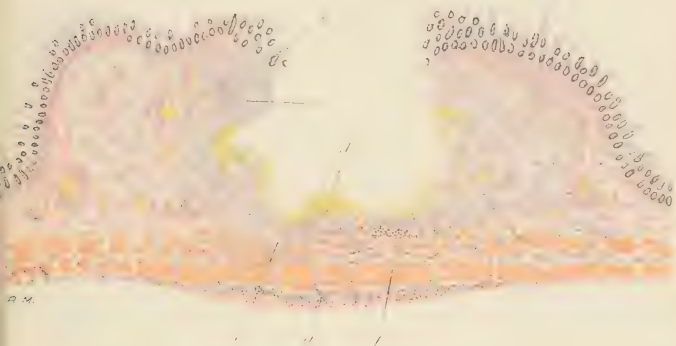


FIG. 179.—Section through an ulcerating Peyer's patch of the small intestine in a case of typhoid fever. Stained with logwood and eosin. ($\times 15$.)

- a.* Normal mucosa with well-stained epithelial tissue.
- b.* Similar tissue at margin of ulcer, not so well stained. (In this case the lymphoid tissue is not so widely affected.)
- c.* Cellular lymphoid tissue.
- d.* Floor of ulcer composed of bile-stained and necrosed tissue; this soon disappears.
- e.* Layer of non-striped muscular tissue, infiltrated and in process of breaking up.
- f.* Outer layer of muscle in a condition of cloudy swelling.
- g.* Subperitoneal tissue. Cells more numerous, and fibrous tissue swollen.

the muscle fibre near the floor of the ulcer and the cellular infiltration between the fibres should be made out.

The mesenteric glands and the adenoid or Malpighian corpuscles of the spleen must also be examined for congestion, for infiltration with round cells and multinucleated endothelioid cells, and, in specially stained sections, for the specific bacilli.

TUBERCULOUS ULCER OF THE INTESTINE

366. Tuberculous ulcers are found especially in connection with the solitary glands and Peyer's patches, but they are not confined to these positions. They occur most frequently at the lower end of the ileum, but may extend above this point, and down below the ileo-cæcal valve, sometimes as far as the rectum. In its most common form the tuberculous ulcer is met with in very nearly half the cases that succumb to chronic phthisis.

Naked-eye appearances.—The first evidence of the process is the appearance of small greyish or yellowish points in the substance of the glands, or in the submucous tissue. These rapidly undergo softening, the mucous membrane covering them sloughs away, the caseous material is evacuated, and a small deep ulcer, with thickened and overhanging edges, remains. In the infiltrated area are numerous caseous tuberculous nodules, which give the thickened edge a nodulated appearance. There is usually no great undermining of the edges, such as is found in the typhoid ulcer, and in the smaller ulcers they may even be terraced. The floor and edges are pale in the majority of cases, but there may be slight injection extending from the floor, which is then somewhat vascular. The floor is roughened and nodulated, the nodules being most frequently tinged with yellow, from caseation or bile staining, or both. Several ulcers may be found situated close together, separated only by strips of thickened mucous membrane. They extend laterally until they merge into one another, and a large ulcer is formed, which again spreads in a similar way. In consequence of this method of formation, the large ulcer "presents a sinuous or scalloped outline" (Bristowe). Though the ulcer usually runs transversely, and may spread so as to encircle the intestine, it may run in the direction of the long axis of the bowel.

On the serous surface note the following appearances. Immediately under the ulcer, or in its floor, are numerous firm grey or yellowish rounded bodies, which are evidently situated in the subserous lymphatics. Radiating from this position—the floor of the ulcer—are similar lines of tubercle nodules, forming a many-rayed star. There is considerable thickening of the floor of the ulcer beneath the serous surface, and in this the nodules may be felt as hard shot-like bodies. The ulceration usually extends through the mucosa and submucosa,

the muscular tissue then forming the floor. Eventually the muscular tissue may also be involved.

In consequence of this progressive thickening, perforation very seldom occurs; in some cases there may even be cicatrisation of the ulcer. Where there is great loss of substance the contraction is very great, and a stellate puckered scar results, the puckering being especially well seen on the serous surface. Where the loss of substance has been very extensive, the cicatrisation may cause considerable narrowing of the bowel.

Harden (§§ 57 (*a*) and 58, 60, or 63), stain (§§ 102, 104, 110 (*b*), and 132 or 183), and mount (§ 195 or 199).

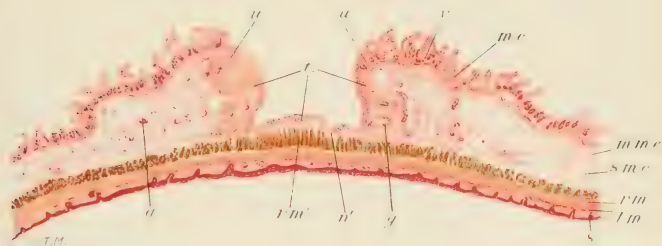


FIG. 180.—Section of tuberculous ulcer of the intestine—ileum.

Stained with picro-carmine. ($\times 30$.)

m.c. Mucosa, which at points (*u.u.*) has given way.

v. Villi, infiltrated and enlarged.

m.m.e. Slightly altered muscularis mucosae.

s.m.c. Submucosa, in which (*t.*) tubercle follicles are present.

In this layer too (*g.*) the blood vessels are considerably dilated.

r.m. Circular muscular fibre, at *r.m'*, swollen and enlarged, and degenerating.

n'. Tubercle follicles situated in this layer.

l.m. Longitudinal muscular fibres.

s. Thickened and vascular serous coat.

($\times 50$).—At the point where the ulcer is situated there is a particularly noticeable increase in the thickness of the submucosa. The edges of the ulcer are covered with mucous membrane up to their margin, but this mucous membrane is markedly infiltrated, so that the villi, which are packed with small round cells, stand out very prominently; beneath the layer in which the crypts are found there

is much round-celled infiltration; scattered through this are tubercle nodules composed of one or more tubercle follicles. Some of these tubercle follicles are beginning to caseate in the centre; others are well formed, and show the regular giant cell system, with its reticular framework and endothelioid and small cells. The floor of the ulcer is rough and nodular, owing to the presence of similar nodules, which in some cases extend into the muscular coat, and also for some distance laterally.

($\times 450$).—Confirm the above appearances, and try to find tubercle bacilli in the giant cells and near the caseating areas.

The mesenteric glands are also usually affected, the tubercle follicles growing first in the cortex. The glands become enlarged and then caseate.

TYPHOID ULCER

1. Direction often longitudinal.

2. Edges undermined, ragged, and can be floated out on water; thin, vascular, and composed of mucosa and submucosa—red.

3. Floor smooth and vascular.

4. Peritoneal surface unaltered, except that it may be inflamed. No thickening and no grey or yellow patches or points.

5. Mesentery unaltered; glands enlarged, vascular, pink, and softened.

6. Perforation more common, both by separation of slough and by direct extension of the ulcerative process. Small opening by which faeces may escape. Peritonitis. Hæmorrhage may occur during either of these processes.

7. Microscopically: A specific inflammation affecting the adenoid tissue;

TUBERCULOUS ULCER

1. Direction transverse (frequently). This distinction is not nearly so characteristic as is sometimes held.

2. Edges not undermined; thick, prominent, nodulated, terraced, or sloping—pale or red, composed of tissue infiltrated with tuberculous nodules.

3. Floor nodular, thickened, irregular, vascular, with pale or yellow points or areas.

4. Sub-peritoneal tissue thickened—small yellow or grey points in the floor of the ulcer, running along the lines of the lymphatics.

5. Mesentery thickened at its attachment to the bowel; glands enlarged, firm and gelatinous on section, or caseous.

6. Perforation, peritonitis, and hæmorrhage, all rare.

7. Microscopically: A specific inflammatory affection also of the adenoid

TYPHOID ULCER—(*continued*)

blood vessels distended, and increased vascularity of the mucosa and submucosa. Dense masses of small round cells—lymphoid cells and leucocytes—with some large multinucleated cells, the latter of which are derived directly from endothelial cells. A line of demarcation is formed, and abscess results. It begins in the solitary glands and other lymphoid tissue of the mucosa and submucosa.

8. Extension takes place laterally, or in depth.

9. Heals by granulation, the thin edges falling on to, and uniting with, the granulating floor of the ulcer.

10. Leaves a smooth, often depressed, pale, anæmic or pigmented cicatrix, covered by a layer of epithelium, but no gland tissue. Seldom breaks out afresh, relapse being due to the affection of adenoid patches previously little damaged.

TUBERCULOUS ULCER—(*continued*)

tissue and the mucous membrane, ending in caseation and connective tissue formation; vascularity of mucosa and submucosa; increase of connective tissue cells and lymphoid cells; tubercle nodules typical or caseating. It begins in the mucous membrane, and, like the typhoid lesion, is due to direct contagion or infection.

8. Extension usually takes place laterally.

9. Heals more rarely.

10. Leaves a puckered cicatrix in which are grey or white nodules. Often breaks out afresh.

WAXY INTESTINE

367. Waxy or amyloid degeneration of the intestine very frequently occurs in general waxy disease. It gives rise to watery diarrhœa and exhaustion, to which the patient succumbs. The change is most frequently and first seen at the upper part of the ileum and the lower part of the jejunum, though the mucous membrane of the whole alimentary tract may be more or less affected.

Naked-eye appearances.—The mucous membrane is pale, and has a peculiar smooth and glossy look, and a fine velvety feel. On pouring a watery solution of iodine (§ 133) over the surface, a number of dark mahogany-brown points, corresponding to the vascular loops of the villi, make their appearance. Between these points the normal tissues are stained yellow by the iodine. In the large intestine the dark staining is more diffuse, owing to the absence of villi and the presence of a dense vascular plexus in the mucous membrane.

Harden (§§ 57 and 60 or 63); mount one section unstained (§ 195), and stain one (§ 117), another (§§ 102, 103, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—The waxy change is most marked in the capillary plexuses of the villi, the vessels of which have their walls swollen, hyaline, and stained red-violet by methyl-violet. In consequence of this swelling of the wall, the lumen is considerably narrowed. The middle coat of some of the larger and deeper vessels is also affected. The epithelium on the surface of the villi is often detached and granular, but seldom or never waxy. In some cases there is waxy degeneration



FIG. 181.—Section of waxy intestine. Stained with methyl-violet.
($\times 50$.)

- a.* Capillary vessels of villi of intestine in advanced stage of waxy degeneration.
- b.* Small arterial vessels in mucosa.
- c.* Larger arterioles in submucosa in which the middle coat is distinctly waxy.
- d.* Inner muscular coat.
- e.* Outer muscular coat.
- f.* Subperitoneal and peritoneal coats of intestine.

of the delicate connective tissue fibrils between the bands of non-striped muscle fibre, leading in advanced cases to their atrophy; this may be readily recognised.

($\times 300$).—The evidences of waxy degeneration of the loops of vessels in the villi may be clearly made out. The middle coats of both larger and smaller vessels are similarly affected. The waxy material may be observed between the bands of atrophied non-striped

muscle fibre, which latter, however, are seldom or never waxy; the



FIG. 182. Villus of waxy intestine. Stained with methyl-violet,
($\times 300$.)

- a.* Waxy capillary.
- b.* Epithelium covering villus.
- c.* Epithelial cells lining a follicle.
- d.* Small waxy arteriole leading to capillary network.
- e.* Muscularis mucosae.
- f.* Submucous tissue.

endothelium may be fatty, but never waxy. The epithelium on the

surface of the villi, as already seen, is fatty, granular, and detached, but rarely waxy.

DYSENTERY (BACILLARY FORM)

368. This disease affects, primarily, the large intestine, especially its lower part; but in some cases it occurs higher up, in the lower part of the ileum.

The first indication of the process is swelling, accompanied by redness, of the mucous membrane; on this a viscid or tenacious mucus, streaked with blood, accumulates. The swollen mucous membrane is thrown into folds, along the ridges of which there is well-marked vascularity. At this stage the solitary glands are firm and swollen, and here and there are small hæmorrhages and an accumulation of coagulated fibrinous lymph on the surface. After a few days, sloughs, which again occupy the ridges of the mucous membrane, are formed. These are blood stained, bile stained, or ashen grey and, separating, leave the submucosa bare, very intractable ulcers resulting; these, if the patient lives, are evidence of the chronic form of the disease. Small ulcers are also found in the position of the solitary glands. These ulcers in the acute condition are deep, from the thickening of the surrounding mucous membrane, and around each is a zone of active congestion, and frequently, also, a number of small hæmorrhages. The contents of the intestine in this condition, consisting of mucus, altered blood, and shreds of sloughy tissue, emit a very foul odour, and in acute cases are teeming with the specific bacilli. These shreds of sloughy tissue are found to be teeming with micrococci and coliform organisms, which have been described by different observers as being the causal agents in the production of this condition. (See Muir and Ritchie, "Manual of Bacteriology").

In still more acute forms the mucous membrane is deep red or livid, and may come away in the form of an almost complete cast of the bowel, usually accompanied by profuse hæmorrhage.

Harden (§ 58 or 60) and stain (§§ 102 or 104 and 117).

($\times 50$ and $\times 300$).—There is first a very great amount of small round-cell infiltration in the tissue around the Lieberkühn's follicles. There is similar infiltration of the solitary glands. Near the margins of the ulcers the infiltration is well marked, especially around the distended blood vessels. Some of the solitary glands are breaking down, and in this way smaller ulcers are formed. The glands of

Lieberkühn are elongated, and are alternately constricted and bulging, the epithelium is in a condition of coagulation necrosis and is frequently in process of being shed. Among the cells around the vessels are the elements of a coagulum—coagulated fibrin and red and white blood corpuscles. Around an ulcer, both in its floor and at its margins, are numerous round cells, infiltrating the whole of the tissues, whilst large swollen endothelial cells are sometimes described as being present in the lymph vessels in the neighbourhood of the ulcer. In the methylanilin-violet stained specimen, masses of micrococci and coliform organisms are met with, still attached to the surface of the mucous membrane, especially where sloughing is beginning.

Under the high power note that the cellular infiltration is made up largely of plasma cells. As the process becomes more chronic, it will be noted that the connective tissue cells evidently undergo marked proliferation.

AMÆBIC DYSENTERY

369. In the amœbic form of tropical dysentery the *Entamœba histolytica* is found in the fæces, which should be examined as fresh as possible and before the reaction becomes acid. It is also found in the intestinal canal, both in the very active amœboid form and in what is called the resting stage.

($\times 1000$).—The active amœboid organism often found during the early or acute stage of the process resembles the active form found in tropical abscess of the liver (§ 251); it is an organism of considerable size (12 to 30 μ in diameter), is oval, pyriform, sometimes with a more or less well-marked constriction in the centre; it has a highly refractile ectoplasm and a granular endoplasm. When fixed and stained, the nucleus is usually pushed to one side, and vacuoles containing red corpuscles, leucocytes, bacteria and other minute foreign particles may be seen embedded in the granular endoplasm. It can be best examined in the fresh stool from a case of dysentery, either at once or after hardening in bichloride of mercury, embedded in celloidin and cut into thin sections. This organism differs from the *Entamœba coli*,—often met with in the intestine,—which has a more distinct nucleus containing larger chromatin masses and is surrounded by a highly refractile nuclear membrane. Further, in the *Entamœba coli*, the cytoplasm is of the same character throughout,

there being no differentiation into ectoplasm and endoplasm. In the later stages of the disease, when the stools are becoming more normal in consistence, the organism met with is often in the resting phase, the nucleus is less distinctly marked, and may consist of small masses of chromatin distributed throughout the cell or penetrating small buds formed on the surface. Around each of these buds, three, four, or more, a highly refractile cyst wall is formed, the cysts becoming separated from the rest of the cell, the remnant of which undergoes disintegration. These cysts are extremely resistant,

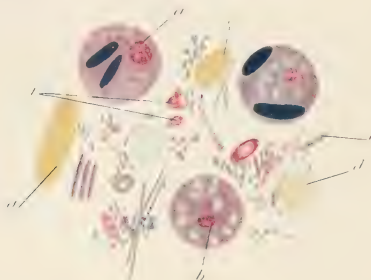


FIG. 183.—Fæces from a case of dysentery containing *Entamoeba histolytica* (resting stage). Stained by Benda's method. ($\times 1000$.)

- a. Rounded amoeba with eccentric nucleus, a few vacuoles and large deeply stained organisms.
- b. A similar amoeba with more vacuoles but no ingested particles.
- c. Fragment of partly digested food.
- d. Nucleated epithelial cell.
- e. Bacteria, bacilli, cocci, etc.
- f. Sarcina.
- g. Fragment of partially digested muscle.

and probably maintain the continuity of the species outside the body. The *Entamoeba histolytica* in its active amœboid form appears able by its tough membranous pseudopodia to push its way into the mucous membrane of the large intestine, especially the rectum, the lower part of the ileum, and the flexures. Once it is ensconced in the tissues, small soft oedematous-looking swellings soon appear on the mucous surface; in the centre of these appear minute ulcers, first in the mucous membrane and then extending into the submucous tissue. These small ulcers undermining the swollen mucous membrane may

gradually increase in size by a process of progressive necrosis until several may run together. The acute hæmorrhagic condition and dense infiltration so characteristic of the bacillary form of dysentery are seldom present. As these tissues slough, ulcers with irregular overhanging margins and well-marked underlying excavations are formed. Liver abscess is often associated with this condition.

Harden (§ 58, 61, or 63) a piece of the intestine, including the thickened and necrotic tissue (§ 251), stain (§§ 115, 117, 126, 110, and 148), and mount (§§ 193 and 199).

($\times 50$).—The swollen or overhanging mucous membrane is somewhat irregularly and imperfectly stained, the tissue elements are usually separated by fluid, and there is sometimes a slight increase in the number of nuclei between them, but this is seldom a marked condition. In the mucous membrane, in the submucous tissue and even in the muscular tissue, the active amœbæ may be seen surrounded by a few cells of which the nuclei are broken up and in which even the protoplasm is undergoing disintegration. At some little distance from the amœbæ there appears to be some proliferation of the connective tissue cells but little migration of leucocytes. The amœbæ may be unaccompanied by any other organisms, but after the ulcerative process has gone on for some time secondary infection by bacteria from the intestine is of frequent occurrence. The nuclei of the tissues are badly stained, and the cells often consist of little more than masses of granular débris.

($\times 1000$).—The reaction of the amœbæ to the necrotic and liquefactive processes should be carefully studied, and it should be noted that although the connective and other tissue cells may be stimulated to divide or may be "killed" perhaps by a toxin formed by the parasitic amœbæ, there is little evidence of vascular reaction or migration of leucocytes to the zone in which the parasite is acting, and therefore little suppuration. The amœbæ may be found at some distance from the floor of the ulcer, pushing their way into the submucosa and even into the muscular coat of the intestine, and the changes around them are always in the first instance of the same (necrotic) type. When we have any evidence of acute inflammatory (in contradistinction to simple necrotic) reaction, such reaction is usually the result of some secondary infection by micro-organisms that have found a nidus in the intestine and a specially favourable field of operations in the necrosed and partially devitalised tissue.

TUMOURS OF THE ALIMENTARY TRACT

370. *Lipoma* is met with in the mucous membrane of the cheek and lips, in the œsophagus and stomach, and in the intestine.

Fibroma, in the tonsils and salivary glands, and in the other parts of the alimentary canal, affected by lipoma.

Myoma, in the œsophagus, stomach, and intestine.

None of the above three forms are common in the œsophagus; they are more frequently seen in the stomach, but are comparatively rare in the mucous membrane of the intestine, where, however, they may occur in the form of polypoid tumours.

Myxoma, in the form of mucous polypus, in the uvula and soft palate, in the nares and in the œsophagus. Myxomatous tumours also grow in the salivary glands, in which also *chondroma* frequently makes its appearance.

Lymphangioma is found in the tongue and lips, and *hæmangioma* in the lips, tongue, and intestine.

Papilloma is rarely seen in the œsophagus, but is comparatively common in the stomach.

Simple adenoma usually occurs in such structures as the mucous glands, but it is also found in the intestine, especially in the rectum.

Ranula and other *cysts*, the result of distension of ducts or glands—as, for example, of small mucous glands—occur in the mouth.

Of the malignant growths, various forms of *sarcoma* grow from the jaws, in connection with either the periosteum or bone marrow; in the salivary glands, and very rarely in the œsophagus, stomach, and intestine. *Lympho-sarcoma* is also found in the wall of the stomach.

Squamous epithelioma (primary) develops in the lips, tongue, and gums, very frequently in the œsophagus, especially at the junction between its lower two thirds, and in the rectum near the anus.

Malignant adenoma or *adenoid cancer*, like the other cancers, is usually found at the pyloric end of the stomach. In the colon, where it frequently occurs, it specially affects the flexures.

Carcinoma may occur in the salivary glands and tonsils, but its most frequent positions are the stomach—the pyloric end—and the rectum. In both positions it is usually primary, and may be of the scirrhus, the encephaloid, or the colloid form. It will be described in the section on Tumours. In carcinoma of the stomach the

tendency to softening and hæmorrhage must be specially borne in mind. Cancerous infiltration of the submucous tissue is frequently very clearly marked. In most cases of cancer of the pyloric orifice there is, naturally, as the result of irritation, catarrh of the stomach, with dilatation and hypertrophy of the muscular walls, owing to the obstruction of the pyloric orifice. (See Chapter XIV.)

Mixed tumours specially affect the jaws and the salivary glands. The occurrence of *gummata* in the tongue and pharynx, and of *tubercle* in the tongue and tonsils, should be borne in mind.

For *parasites* of the alimentary canal, see Chapter XV.

PERITONEUM

371. For structure and inflammation of the peritoneum, see § 221.

TUBERCULOSIS OF THE PERITONEUM

372. A non-caseating tuberculous process is very frequently met with in the peritoneum in the general tuberculosis of children. This is perhaps one of the best possible positions in which to examine young tubercle.

Hold a piece of the peritoneum up to the light, or lay it out on a dark background, and in it will be seen a number of minute white or cream-coloured points, very like those met with in tubercle of the pia arachnoid, say at the base of the brain. Spread out on cork, harden in Müller's fluid, diluted with water to one-half the ordinary strength, stain (§§ 102, 103, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—Along the course of the small blood vessels, at irregular intervals, are masses of cells which appear to have a fairly definite boundary. The cells vary in size; some are small and round, whilst others are endothelioid, and contain several nuclei. Along with these masses are lines of cells which apparently still follow the course of the vessel, whilst at other points there appears to be proliferation of the endothelial cells on the trabeculæ.

($\times 300$).—It appears that the endothelioid cells in the perivascular lymphatic spaces are at certain points undergoing proliferation, and that this cell growth is really the early stage of tubercle formation, already described (§ 246). There are no giant cells, properly so called,

and the greater number of the changes take place at intervals along the line of the artery, but not of the vein.

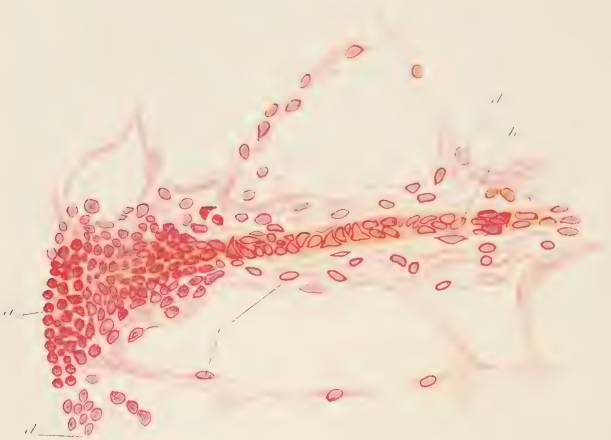


FIG. 184.—Early acute tubercle of the peritoneum, from a child.
Stained with picro-carmin. ($\times 300$.)

- a.* Young tubercle growth. Endothelial cells growing within the peri-arterial sheath, and also on the peritoneal surface.
- b.* Artery, along the course of which the proliferating endothelial cells may be seen.
- c.* Fibrous trabeculae.
- d.* Proliferating endothelial cells lying on these trabeculae.

373. Chronic tuberculosis of the peritoneum, characterised by matting together of the intestines, and puckering and thickening of the omentum, occurs very frequently in connection with tubercle of the intestine. The principal features of this condition are extremely slow growth, perfectly formed giant cell systems, and chronic peritonitis.

374. Waxy change in vessels may be readily studied in the peritoneum, as may also the vascular changes in septicæmia, anthrax, and similar conditions.

375. *Cancer*, especially the colloid form, and *sarcoma* both occur as secondary growths in the peritoneum. (See Chapter XIV.)

CHAPTER XI

BONE AND JOINTS

STRUCTURE OF NORMAL BONE

376. In order that the pathological changes in bone may be understood, the following brief résumé of the appearances present in normal bone (*a*) in a cartilaginous basis, and (*b*) in connection with periosteum, is given.

Naked-eye appearances.—On vertical section through a normal developing bone, the radius, say, in which the epiphysis has not yet become united to the shaft, the end is seen to consist of cancellated or spongy bone; the epiphysis, which is also cancellous, is invested on one surface by articular cartilage, on the other by a narrow blue line of what is known as the intermediary cartilage. In very early or foetal life this latter is much thickened, and is made up of two kinds of cartilage, hyaline—the remains of the foetal epiphysis—and the intermediary cartilage proper, in which calcification is sometimes taking place. Beneath this comes the bone of the shaft.

Soften the bone (§ 75, 76, or 80), cut (§ 82 *et seq.*), stain (§§ 102, 104, or 110 (*b*), and 132), and mount (§§ 193 and 199).

The epiphysis is made up of spongy bone in which, on the homogeneous-looking trabeculae, lie numerous small nucleated cells—known as osteoblasts. Running through spaces left between the trabeculae are blood vessels, all of which are surrounded by small nucleated cells,—connective tissue cells, and leucocytes. When development has not gone far, these trabeculae, in place of being homogeneous, are evidently bars of cartilage in which calcification is beginning: as development becomes more complete, the bony matrix is gradually laid down on these trabeculae and the cartilage disappears (by absorption). Beneath the bony trabeculae of the epiphysis is (in the foetus) a layer of hyaline cartilage, composed of a homogeneous matrix, in which the dividing

cartilage cells, with their distinct capsules, may be readily seen. Then comes the intermediary cartilage, in which the matrix is distinctly calcified at its lower part, and the flattened cells have a very characteristic arrangement in longitudinal rows or columns. Near the surface these cells are comparatively small, but as we approach the developing bone

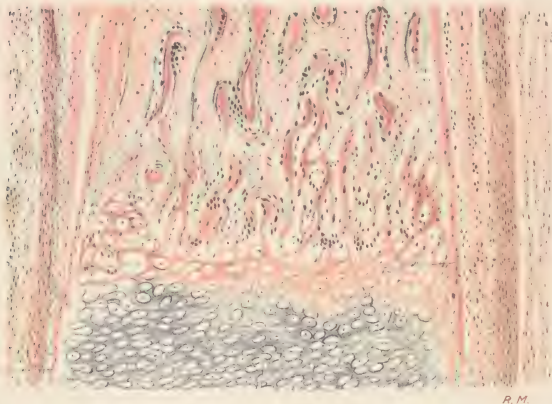


FIG. 185.—Section of end of long bone taken from a three months' old foetus, showing development of bone from cartilage. Stained with eosin and logwood. ($\times 50$.) (H. A. Thomson.)

- a.* Columns of cartilage cells at the end of the bone.
- b.* Periosteum with its fibrous and cellular layers.
- c.* Transition of cartilaginous into bony matrix. In this the cartilage cells are small and atrophied. Immediately above this the cartilage spaces open into spaces containing blood vessels and osteoblasts.
- d.* Bony trabeculae.
- e.* Vessels in spaces.
- f.* Osteoblasts or bone-forming corpuscles lining these spaces.
- g.* Muscular tissue.

of the shaft, they are much larger and usually cubical in shape. They are contained in spaces of considerable size, the lowest of which open into long marrow cavities, as the spaces between the bony trabeculae are called.

In the bones of very young children the trabeculae are composed

of calcified cartilage; they are covered with osteoblasts, whilst here and there are large multinucleated cells—chondroclasts—similar in all respects to the absorbing giant cells or osteoclasts (to be described immediately), and to the giant cells met with in myeloid sarcoma.



FIG. 186.—Section of periphery of long bone taken from a three months' old foetus, showing development of bone from periosteum. Stained with eosin and logwood. ($\times 300$.) (H. A. Thomson.)

- a. Fibrous layer of periosteum.
- b. Osteogenic layer of cells by which bone matrix is formed.
- c. Blood vessel in periosteum surrounded by leucocytes.
- d. Outer fibrous (or muscular) layer.
- e. Cells lining one of the marrow cavities in which a vessel runs.
- f. Do., seen in transverse section.
- g. Bone corpuscle not branched.
- h. Branched bone corpuscle.

In the older bone, or further away from the cartilaginous surface, are regular osseous trabeculae on which are arranged the small nucleated bone-forming osteoblasts, and the large multinucleated bone-absorbing osteoclasts. In the longitudinal marrow spaces are well-formed blood vessels. Wherever there is a *cartilaginous* matrix, we

have the same conversion of the cartilaginous trabeculæ; first they become calcified through a deposition of lime salts in the matrix and in the capsules of the cells, and then, laid down on these cartilaginous trabeculæ, and gradually taking their place, are regular bony layers covered with osteoblasts, which play an important part in the formation of the bone proper. Osteoclasts or giant cells rest in the pits or lacunæ described by Howship, each of which appears to have been hollowed out by its own cell.

Around the bone is the periosteum which forms a vascular fibro-cellular sheath, a most important factor in the nutrition of the bone. Its outer layer is dense and fibrous, and contains but few cells, but within this is a bone-forming or osteogenetic layer which is composed of nucleated cells arranged in a *fibrous* matrix. The cells near the surface are rounded and comparatively small; near the centre they become much larger and often more or less spindle-shaped. In this region the fibrillated matrix becomes distinctly osseous, and there are marrow or Haversian spaces lined with osteoblasts; surrounding each Haversian space is a somewhat laminated bony tissue, with lacunæ containing branched bone corpuscles or modified osteoblasts.

The different modes of bone formation (in cartilage and periosteal) must be carefully borne in mind in the study of bone repair and of rickets. In both modes, whether in the periosteum or in the Haversian canals, the osteoblasts are associated with growth, they form a matrix which is ultimately converted into bone; the osteoclasts, on the other hand, play an important part in the removal of bone already formed. There is a continual bone formation, always accompanied by bone absorption.

REPAIR OF BONE—CALLUS

377. Callus is the new or cicatricial tissue that is formed to make good a fracture in a bone. Although met with every day by the surgeon in cases of simple fracture, it very rarely comes under the observation of the pathologist, unless produced experimentally upon the lower animals. The conditions under which experimentally produced callus occurs differ very materially from those under which it is formed in the human subject. Of these conditions the most important is the impossibility of maintaining the fractured limb of an animal in one position for any length of time. In consequence of this, it is almost impossible to obtain accurate and permanent apposi-

tion of the fractured ends of the bone; the external, provisional, or supporting callus, *i.e.* that around the bone, forming a kind of natural splint, is produced in excess (owing to excessive irritation of the surrounding tissues), and it and the tissue between the ends of the bone become cartilaginous. The part between the ends of the bones is spoken of as the intermediate or permanent callus; that in the hollow of the shaft—the internal callus—is also provisional in character, and is ultimately absorbed.

Naked-eye appearances.—Examine the callus from the tibia of some small animal—a rabbit, for instance—ten or twelve days after fracture. Make a longitudinal section through the centre of the bone. The extravasated blood, which was thrown out at the time the bone was broken, and which, as in a healing wound of the soft tissues, is such an important feature during the first six or eight days, has now to a great extent disappeared; it has been absorbed, having played its part as a scaffolding. Around the fractured ends of the bone, and merging into the periosteum, is a pale mass which extends for some distance above and below the fracture, and apparently involves the surrounding tissues to a considerable extent. At first this mass consists almost entirely of cartilage, developed from the granulation tissue which is formed around the broken ends of the bone, just as in any other healing wound (§ 225). Near the bone, soft, vascular, fibro-cellular tissue may be made out, blending with the remainder of the callus. The outer surface of the provisional callus is usually much pinker, as it is more vascular, than any other part; it thus early appears to form a provisional periosteum.

Passing for some distance into the medullary cavity is a mass of granulation tissue, in which may be found small cartilaginous islets. The only evidence of ossification as yet met with is in the position in which one would expect to find it, *i.e.* near the sound bone where the periosteum is least altered, and near the vascular surface, at the extremities of the spindle-shaped callus (the points at which there is least movement of the tissues, *i.e.* where they are most at rest); and here, with the aid of a magnifying glass, delicate trabeculae of bone may be distinguished running apparently from the sound bone, at right angles to the surface, in the line of the new blood vessels.

Prepare (§ 75 or 76), embed and cut (§§ 91 and 92), stain (§§ 103, 104, or 110 (*b*), and 132), and mount (§§ 193 and 199).

($\times 10$).—Notice that at the fractured ends the bone has become



FIG. 187.—Section of a fractured bone in which provisional callus is well formed. Stained with eosin and hæmatoxylin. ($\times 10$.)

- a.* Granulation tissue.
- b.* Cartilaginous tissue.
- c.* Osteoid tissue of internal callus.
- d.* Osteoid tissue of intermediate callus.
- e.* Cartilaginous tissue.
- f.* Osteoid tissue.
- g.* Vascular subperiosteal layer of external callus.
- h.* Normal periosteum.
- i.* Fatty marrow in shaft of long bone.

Later, lime salts are laid down in fibrous, osteoid, and cartilaginous matrices as in normal bone formation.

decidedly more porous, and there is a condition practically of rarefying osteitis (§ 380). The trabeculae are thinned, the canals are wider, and are filled with a mass of granulation tissue which passes for some distance into the central medullary cavity, and, unlike the provisional callus, remains non-cartilaginous. It is made up of a mass of young cells, which can scarcely be distinguished from the ordinary subperiosteal and medullary cells; in this tissue ossification goes on, just as in the growth of a normal bone. Between the ends of, and around the bone, the callus is composed, principally, of a mass of young cartilage cells embedded in a distinct matrix, the cells proliferating and the matrix becoming darkened and granular as calcareous salts are deposited. This cartilaginous mass is for the most part well supplied with blood vessels. It is extremely vascular near the surface of the bone, and still more so on the free surface, where there is a species of new periosteal tissue developed in the form of a layer of dense pink fibrous tissue. Beneath this is the subperiosteal tissue, a layer of small round cells, unlike the cartilage cells in that they are not surrounded by a regular homogeneous matrix. In these two vascular areas of the new cartilage the process of ossification begins, then bony trabeculae may be seen running parallel with the vessels. In this section nothing further can be seen; but if the process be followed out in other preparations, made where the union is more advanced, it will be found that the provisional callus eventually becomes bony throughout, the process of ossification extending from its two extremities, along the inner and outer surfaces, forming two layers, which at first (until they meet in the centre) enclose a mass of cartilage.

($\times 300$).—In the medullary canal, near the fracture, the amount of fatty medulla is usually diminished; the internal callus is composed of embryonic connective tissue, made up of cells with large nuclei, and only a small quantity of periplast. These cells are very similar to the cells met with in the subperiosteal layer. This is the only position in which the tissues are perfectly at rest, and, therefore, the only position in which, as a rule, ossification goes on directly in fibrous tissue without the intervention of cartilage.

Next examine the intermediate callus, or that between the ends of the dense bone. It is composed, at this stage, principally of cartilage, the cells of which are undergoing a process of division, whilst the matrix is usually calcified, and therefore extremely granular. In some

cases, however, the amount of cartilage is comparatively small, and its place is taken by a fibro-cellular structure, almost like that found in a young cicatrix.

The external provisional callus, or that outside the bone, like the intermediate callus described above, is almost entirely cartilaginous. In this observe the gradual transformation of the proliferated cartilage cells into bone corpuscles; the granular appearance first of the cartilage capsule, and then of the matrix, is due to the deposition of calcareous material. Near the bone the embryonic blood vessels, composed of double rows of cells, as in ordinary granulation tissue, run at right angles from the Haversian canals of the bone into the callus. Similar vessels run from the surrounding tissue on the free surface. Note the appearance of the spicules of bone along the course of these vessels. The further ossification goes on regularly, and may be studied along with that of normal bone.

If the bone can be kept perfectly at rest, the amount of irritation, and consequently the amount of callus is small, and the process of repair takes place without the intervention of a cartilaginous splint.

In a compound fracture, on the other hand, there is the formation of an excess of medullary and subperiosteal (granulation) tissue as the result of greater irritation, and thus ossification goes on just as in the growth of the normal bone, rapidly and simply, without the formation of any cartilage. Absorption of excess of bone ensues, and the outlines of the medullary cavity and of the bone may be restored.

RICKETS

378. Rickets must be looked upon as a disease of an essentially constitutional character, the result of malnutrition. It is most frequently observed in badly nourished children, from one year old and upwards, the period during which the bones in which the changes associated with rickets are most marked, are being most rapidly developed. These changes are best seen in the long bones, especially at their points of junction with the various cartilages, but the flat bones of the head, and even the spongy bones of the spinal column, may undergo considerable alteration.

The ends of a rickety bone are enlarged and clubbed, and the shaft is often thickened, especially in the concavity of its curve, which is usually greatly exaggerated, a buttress of new bone being thus formed.



FIG. 188.—Longitudinal section of the enlargement at the sternocostal junction in a case of rickets. Stained with eosin and logwood. ($\times 15$.)

- a.* Normal sternocostal cartilage.
- b.* Irregular rows of calcifying cartilage cells.
- c.* Irregular calcification in thickened cartilage.
- d.* Cartilage with but slight calcification.
- e.* Area of new-formed but irregular bone.
- f.* More regular osteoid tissue with imperfect calcification.
- g.* Osteoid matrix.

In the chest of a rickety child it may be observed that at the junction

of the ribs with the cartilages on both sides of the sternum there is a series of enlargements or knobs, giving rise to the well-known "rosary" or beaded appearance. External to the "rosary" is a groove, due, apparently, to the retraction of the softened and less resistant ribs during the inspiratory effort. As the softened ribs are flattened or drawn in, the sternum is rendered more prominent. In a typical rickety bone, such as the radius, the enlargement extends above the thickened and irregular epiphyseal cartilage. If the muscles be stripped from the shaft of the bone, the periosteal layer will be found thickened and very vascular; and the shaft in place of being dense is almost like the spongy tissue of the extremity. In consequence of these changes the bones are very soft and friable, are readily bent, and may be easily cut with a knife; they are usually much shortened. Infractures, or "green-stick" fractures, frequently take place, especially in the upper limbs, and the epiphyses are often displaced.

Make a vertical section through the shaft with its epiphyses or a rib with its "external" cartilage, and notice the great increase of translucent or bluish cartilage, which, in place of forming thin regular layers on the articular surface and between the epiphyses and the shaft, forms broad, irregular, somewhat porous belts (in which small islets of calcifying tissue are scattered) dipping into the main mass of calcifying tissue. In these islets of calcifying tissue pink and yellow points are seen; these are the calcifying centres, the pinker ones containing numerous blood vessels. The cut surface of the shaft is exceedingly red and vascular, the bony lamellæ are thin and friable, and it is evident that rapid absorption is going on; the marrow is relatively large in amount, and is red and gelatinous instead of being yellow and fatty.

Treat pieces of the cartilage and bone from near, say, the sternocostal articulation (§ 68), stain (§§ 102, 103, or 104, 110 (*b*), 132, and 133), and mount (§ 195 or 199).

($\times 15$ and $\times 50$).—In the thickened belt of cartilage with the irregular calcareous and bony layer beneath, there is great proliferation of the cartilage cells, some of which have a regular arrangement, though by far the greater number are grouped without any attempt at arrangement, either as regards columns or size, and in many cases there is comparatively little matrix. In the small yellow opaque points calcification is going on both in the matrix and in the capsules of the cells. The patches of calcified cartilage are not arranged regularly, but

crop up indiscriminately. Blood vessels also make their appearance at irregular intervals in the cartilage, and, closely following them, appear spaces similar to those met with in ordinary bone, many of which are lined with a regular layer of osteoblasts; thus true bone, or a structure which very closely resembles it, is formed. Even in the midst of the bone formed in this position, masses of irregular cartilage cells may still be seen.

($\times 300$).—The above appearances must be observed more closely, the great irregularity in the size of the cells, in the matrix, and in the calcification of the matrix; the calcification of the cartilage cells at certain points, their proliferation and apparent transformation into osteoblasts. Even where true bone is formed, it appears to be laid down without any attempt at order or regularity, and bone, calcified cartilage, and true cartilage are mixed up, apparently indiscriminately. Here, then, the chief point to be noted is the enormous and irregular increase of cartilage, with irregular and deficient bone formation.

($\times 50$).—Now examine the piece of the shaft or rib. Under the fibrous layer of the periosteum is a great increase in the number of small round cells or osteoblasts, which form a thick deeply stained layer. In the deeper part of this cellular mass a few trabeculae, partly fibrous and partly calcified, may be seen. These trabeculae form an open network, and are seldom or never perfectly ossified; they consist rather of a calcified fibrous matrix. Beneath this *osteoid* tissue (very like that seen in an osteoid sarcoma) comes the true bone, somewhat loose in texture and irregular in structure, in some cases almost like spongy bone. In this tissue the number of vessels and osteoblasts is always very great, but the osteoclasts are not markedly increased in number.

($\times 300$).—The round cells, or osteoblasts, along with the numerous blood vessels, are readily seen, not only beneath the fibrous layer, but between the granular-looking trabeculae, and in the spaces between the osseous trabeculae. In normal bone these osteoblasts grow slowly, and form around them periplasts, which gradually become calcified. In the case of rickets, however, these osteoblasts are formed in very large numbers, but any periplast which they may form is always small in quantity and only imperfectly calcified: there is also fine fibrillation of the intercellular substance, parts of which remain fibrous in place of being converted into bone.

In the flattened bones, such as those of the skull, a process similar to that which goes on under the periosteum of a long bone is met with:

but where the weight of the brain presses upon the soft tissue, the bone does not develop, and the skull at that point (occipital or parietal bone) remains very thin. The pelvis may also be deformed in this condition, and curvature of the spine is often met with as a result of the softening and mal-development of the vertebræ.

It is evident from the above description that, although there is great but irregular proliferative activity in the cells, both of the cartilage and of the periosteum, calcification and ossification go on slowly and incompletely. Although little new bone is formed, the process of absorption goes on as usual (sometimes even more rapidly than normal, as the increased quantity of granulation tissue, or red cellular marrow, aids in this process); but as the old trabeculae are absorbed, new ones are formed to take their place. At the end of the developmental period, however, or where the disease gives way to treatment, the bones, when ossification does set in, may become very thick and strong, from the fact that the osteoplastic tissue is present in such large quantities. The bones may be stunted and deformed, owing to the fact that ossification sets in so rapidly that the epiphyses unite at an earlier date than usual, and the child remains stunted and dwarfed. The ridges to which the muscles are attached are very well marked, being drawn out during the *soft* stage.

Sir Thomas Barlow has described an exceedingly acute form of rickets, known as scurvy rickets, which is supposed to be due to constitutional disturbance, associated more or less directly with the administration of unsuitable food. It is characterised by sudden swelling of the bones, especially of the femur (over which there is tenderness or even great pain), œdema, a spongy condition of the gums and petechial hæmorrhages in the skin. After death similar hæmorrhages may be found in most of the soft tissues and under the periosteum, especially at the junctions of the epiphyseal cartilages with the long bones. These hæmorrhages are sometimes very extensive, though it is somewhat remarkable that necrosis seldom or never seems to follow this condition. We have the same cellular proliferation both in cartilage and in the bone, rapid absorption, and irregular and imperfect calcification.

OSTEITIS

379. In bone, as in all other tissue, the manifestations of inflammation are very various, and because of the rigidity of the structure of

bone the results are very different, according as the process is acute or

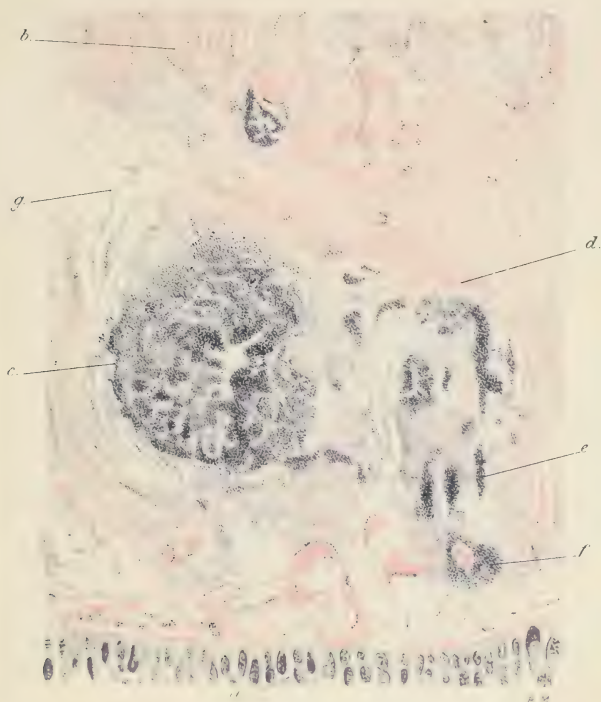


FIG. 189.—Section of bone taken from the lower end of the tibia of a patient suffering from septic osteomyelitis. Stained with eosin and logwood. ($\times 20$.) (H. A. Thomson.)

- a.* Cartilage cells and matrix.
- b.* Bone trabeculae surrounded by osteoblasts.
- c.* Small abscess (embolic) near the end of the bone.
- d.* Compressed and fibrous tissue around the abscess.
- e.* Marrow spaces filled with leucocytes along the line of the vessels.
- f.* Transverse section of one of the trabeculae with leucocytes and proliferating osteoblasts around it.

chronic, occurs in the periosteum or in the bone itself, or is simple or specific.

From the fact that the shaft of the bone, especially its surface, is to a great extent nourished by vessels that run into it from the periosteum, whenever the periosteum is separated from the bone by accumulations of fluid or pus, the nutritive supply being cut off from the shaft, the uncovered section of the bone dies, and forms a "sequestrum" or dead mass. The periosteum, still carrying on its bone-forming functions, often somewhat irregularly, forms a case around the sequestrum, which, however, acting as a foreign body, keeps up a certain amount of irritation; and suppuration—the result of the admission of micro-organisms to the area of dead tissue—is again set up, or, it may be, is kept up from the first. The pus makes its way to the surface by the shortest available route, an opening or sinus is formed, and the constant discharge keeps this open. Abscesses may also form in bones, especially in the spongy tissue at the ends. Such abscesses, occurring in septic osteomyelitis or inflammation of the bone marrow, are usually embolic, the result of the impaction of septic emboli in the vessels which run in the marrow spaces of the open cancellous tissue.

In certain chronic inflammations where the process of bone formation goes on more rapidly than the process of absorption, the trabeculae may become enormously thickened, and sclerosis of bone may result. In other cases the process of absorption predominates, resulting in a rarefying osteitis; whilst in other cases again—as in tuberculosis or caries—there is, as the result of the formation of tuberculous nodules, a gradual absorption of bony trabeculae (see § 381), cutting off of the blood supply from other portions of the bone, caseation, and formation of a cold abscess.

RAREFYING OSTEITIS

380. Rarefying osteitis must be looked upon as a process rather than as a distinct disease, since it occurs in a great variety of inflammatory conditions. It is almost invariably met with at the end of a bone after amputation, in absorption of the vertebrae by pressure of aneurisms or tumours, or as a general condition sometimes known as osteoporosis—a term which refers simply to the naked-eye appearances.

Whether the rarefaction be due to general or local inflammation, the results are much the same.

Naked-eye appearances.—The periosteum is usually thickened and

fleshy, and may be highly vascular. On longitudinal section the bone is found to be extremely vascular, the dense layer near the surface may be very thin, the marrow spaces are large, and the trabeculae are not only diminished in thickness, but are exceedingly rough and irregular, and the spongy tissue is open and friable. Within the spaces the medulla is red and gelatinous.

Prepare a piece of the porous bone taken from the end of a stump (§§ 75 and 79 or 80), stain (§§ 102, 103, 110 (*b*) and 132 and 133), and mount (§ 195 or 199).

($\times 50$).—Near the free extremity of the bone the Haversian canals are usually undergoing great enlargement, and their walls are

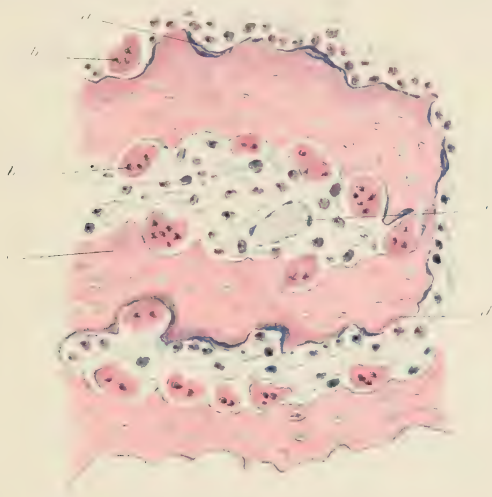


FIG. 190.—Rarefying osteitis. Section of bone stained with fuchsin and methylene-blue. ($\times 300$.)

- a.* Howship's foveolæ,
- b.* in which are lying giant cells or osteoclasts.
- c.* Older bone in which are osteoclasts lying in Howship's foveolæ.
- d.* Newer bone lying near which are osteoblasts.
- e.* Blood vessel.

ragged and irregular. This is most marked at the very extremity, at which point the trabeculae project as fine spicules, and the spaces open into one another. The vessels are dilated, and are surrounded

by a large number of leucocytes, seen as small deeply-stained points. These leucocytes appear to be playing the part of osteoclasts. The whole structure of enlarged vessels and leucocytes has the appearance of a mass of granulation tissue. In addition to the leucocytes, the true osteoclasts (or multinucleated giant cells) are very numerous. In the periosteum the vessels are dilated, there is great extravasation of leucocytes and proliferation of the osteoblasts. Very frequently there appears to be a superficial formation of bone going on in connection with the deep layer of the periosteum, and blood vessels may be seen dipping down into the newly formed bone, and running in between the trabeculae, which are being eroded by the large multinucleated osteoclasts.

The absorption of bone is going on more rapidly than its formation, so that the trabeculae are thin, or in some cases broken down, several canals opening up into one. This absorption appears to be due to the phagocytic or scavenging action of leucocytes that have escaped from the vessels under stimulation during the process of inflammation, and it has even been suggested that many of the giant cells may be nothing more than leucocytes that have combined to form a plasmodium or multinucleated mass of protoplasm, by which the bone is attacked more readily. Under excessive stimulation the osteoblasts are said to act in the same manner.

($\times 300$).—Note the fibrous layer of the periosteum; beneath this the osteogenetic layer is extremely vascular, and from it small vessels, accompanied by a number of small round cells, may be seen passing in between the bony trabeculae. Lying on the trabeculae are numerous deeply stained round cells: these are the osteoblasts, which eventually become transformed into the branching bone corpuscles. In this region the giant cells or osteoclasts are rare.

Nearer the rarefied bone the Haversian canals are much enlarged and very irregular; this irregularity is due to the excavation which extends from the main cavity outwards into the bone of the surrounding Haversian system. These cavities, whether shallow or of considerable depth, usually contain an excessive number of leucocytes, especially in the immediate neighbourhood of the distended vessels. Where the excavation is going on very rapidly, or where it is far advanced, numerous osteoclasts may also be seen lying in large cup-shaped depressions (Howship's foveolae or lacunae) all along the line of erosion. These numerous foveolae, with their contained giant cells,

are simply an exaggerated phase of what is met with in normal bone, which is always undergoing a certain amount of absorption. In the pathological condition, however, the striped margin which is seen in the giant cell of the normal bone is very frequently absent. In the immediate neighbourhood of the giant cell the lime salts are apparently removed before any other elements of the bony tissue are affected.

In rarefying osteitis there is increased absorption of bone, unaccompanied by a corresponding new formation; but it must be remembered that new formation of bone invariably goes on to a certain extent in the deep or vascular layer of the periosteum, and that after the rarefying process has continued for some time the formative process may again predominate, an osteo-sclerosis resulting. This occurs especially in osteitis deformans.

TUBERCULOUS CARIES OF BONE

381. Tuberculous caries may be looked upon as a rarefying osteitis, accompanied by, or rather the result of, the formation of tubercle which rapidly undergoes caseation. It is found most frequently in the spongy bones, especially in the vertebræ, in the bones of the tarsus, in the phalanges of the fingers and toes, in the acetabulum, and in the os calcis; more rarely at the ends of long bones. With this condition suppuration is frequently associated, resulting in what is known as cold abscess of bone.

Naked-eye appearances.—There is usually a diffuse yellow infiltration, especially of the spongy tissue; this appears to invade the bone, causing absorption or destruction of the bony trabeculæ.

In the vertebra the whole of the body may be carious, the disease passing entirely through the intervertebral discs into the vertebræ above and below. In advanced cases there is nothing left but a mass of soft caseous or putty-like material, which may be scooped away with a blunt knife or spoon. This is surrounded by a quantity of grey or pink gelatinous granulation tissue, which gradually extends into the bony tissue, filling up the spaces as the trabeculæ are absorbed. In consequence of the softening and absorption, the bones may be very much deformed: they give way to external pressure, and in the spinal column, where the weight of the upper part rests on the softened vertebral bodies, they are crushed, and spinal curvature is the result.

Harden (§ 58 or 63), or if it is not desired to search for tubercle

bacilli (§ 76), stain (§§ 102 or 103 and 147 or 183), and mount (§ 195 or 199).

($\times 50$).—At some distance from the healthy bone the medullary spaces become larger and more vascular, and the giant cells along the margins of the trabeculae are more numerous. In place of the fat cells of the medulla, a mass of granulation tissue is seen, gradually filling the

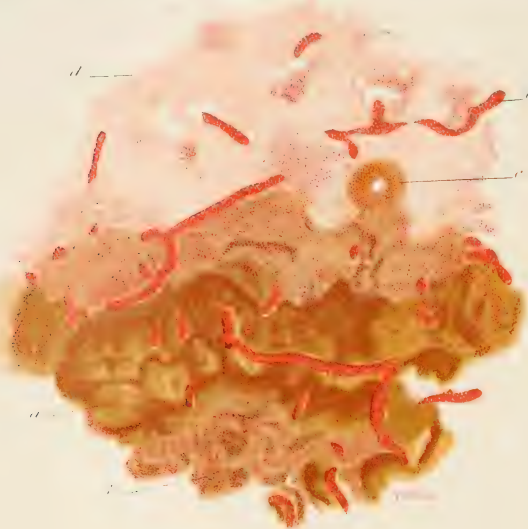


FIG. 191.—Cascating tuberculous infiltration of the spongy bone in the lower end of the tibia. Stained with picro-carmin. ($\times 14$.) (H. A. Thomson.)

- a. Caseous infiltration enclosing trabeculae of dead bone.
- b. Tuberculous granulation tissue with giant cells.
- c. Miliary granulation around medullary blood vessel.
- d. Normal marrow.
- e. Trabeculae of spongiosa, stained with carmine.

somewhat enlarged Haversian spaces. It is composed, principally, of small round cells, and is traversed by a number of vessels. In the mass of granulation tissue are small tubercle follicles, either single or in groups, with their giant cells and typical structure. (See § 246.) This tissue corresponds to the area of gelatinous tissue seen with the naked eye. Where caseation is complete, the bone has entirely disappeared,

or is represented by small detached fragments or spicules, between which are granular shrivelled cells, droplets of fat (stained black with osmic acid, § 135), in fact, simply a mass of caseous debris.

($\times 300$).—Confirm the above appearances. In the granulation tissue tubercle follicles are developed, after which the whole undergoes caseation, as is the tendency in all tubercle formations. Near the centre of the caseous mass the absorption of the trabeculae is complete.

There are also described in connection with bone three other forms of tuberculous lesion—(1) Miliary granulations found in general tuber-



FIG. 192.—Tuberculous necrosis of bone. A vertical transverse section of the upper end of the femur from a case of tuberculous arthritis of the hip, showing a wedge-sequestrum in the cervix, abutting by its base on the epiphyseal cartilage. (H. A. Thomson.)

- a.* Position of epiphyseal plate.
- b.* Articular surface of head.
- c.* Trochanter major.
- d.* Sawn section.

culosis. (2) The chronic circumscribed tuberculous focus of König, which “varies in size from that of a pin-head to that of a cherry, has a translucent periphery of a reddish-grey colour, and appears well defined to the naked eye” (H. A. Thomson). These nodules have all the characteristic appearances of tubercle. They appear to be formed by a fusion of several smaller nodules, which bring about erosion of the bone, caseation takes place in them, and they break down in the centre, just as do all other caseous tubercle nodules; extension takes place at the periphery. (3) A third form is that in which a sequestrum,

often of considerable size, is formed; this, in place of being detached, remains continuous with the living bone. These sequestra are wedge shaped, with the base turned towards the articular surface (they are generally near the ends of the bones); they can usually be seen only on section, and then must be carefully sought for; they are yellow, very dense in structure, and in the spaces tuberculous structure may be made out under the microscope; they are separated from the healthy bone by a zone of granulation tissue, which may, however, in chronic cases be replaced by fibrous tissue.

Before the question of caries is dismissed, it must be mentioned that somewhat similar conditions are met with in syphilis. Here gummata and gummatous granulation tissue take the place of tubercle nodules and tuberculous granulation tissue. We have the same processes of bone absorption, ulceration, and sclerosis, and, so far as can be seen, the processes by which these are determined are almost identical, only the exciting agent being different.

"TUMOR ALBUS," OR TUBERCULOUS ARTHRITIS

382. Synonyms, "Tuberculous Inflammation of the Synovial Membrane," "White Swelling," "Gelatinous or Pulpy Degeneration of Joints."

Tuberculous arthritis may be compared with the tuberculous inflammation of other serous membranes, just as tuberculous disease of the bone may be compared with tuberculosis of the lung; it is most frequently met with in delicate children above three years of age, and occurs in the following joints: most frequently in the knee, then in the hip, elbow, ankle, wrist, and least frequently in the shoulder.

Naked-eye appearances.—There is usually no fluid in the joint; where the disease is somewhat advanced the synovial membrane is invariably thickened, soft, œdematous, and gelatinous, and is usually grey or greyish-white in colour. In some cases exuberant red granulations may be seen projecting from the general swollen mass; the surface may be rough and shreddy, or it may be smooth, in which case small tubercles may be seen standing out prominently from the gelatinous mass.

The other structures in and near the joint become soft and gelatinous, and frequently appear as a mass of pinkish gelatinous material held in position only by the skin. This gelatinous material may fill up the whole of the joint cavity and gradually cause distension;

in such cases the bone is also attacked, the articular cartilages being gradually eroded, and as this takes place the tuberculous tissue gradually makes its way between the bone and the cartilages, slowly detaching the latter from their bony beds. In the knee the semilunar discs may be so infiltrated that they cannot be distinguished from the general mass of tuberculous tissue. This is always best seen at the periphery of the articular surfaces. On section small yellow tubercular points, embedded in the gelatinous mass, may be readily distinguished; these seldom open into the joints unless suppuration has occurred.

The granulations pass into the cartilage, pitting, and in the long-run, absorbing it. They also pass into the articular end of the bone, giving rise to a condition exactly like that already described as rarefying osteitis with tubercle (§ 381). The change then begins in the synovial membrane as a formation of vascular granulation tissue, which gradually invades the surrounding structures. In the granulations are tubercle follicles, which caseate and suppurate.

Harden one piece of the joint, comprising synovial membrane in its fungating condition, a piece of the cartilage, a thin layer of bone from beneath the cartilage (§ 58 or 76), and a piece of the granulation tissue (§ 58), and stain (§§ 102, 103, or 104 and 133), or for tubercle bacilli (§ 183 or 184).

($\times 50$).—The granulation tissue consists of a mass of small round cells, in which a number of blood vessels are ramifying; embedded in it are numerous specially well-developed tubercle follicles. Passing from the under surface of the granulation tissue in the synovial membrane are small processes, which may be seen to run into the substance of the cartilage, gradually absorbing it. In the cartilage itself the matrix appears to be diminished in quantity, whilst there is proliferation of the cells within their capsules, which gradually disappear, so that the cells are no longer encapsuled. The central part of the cartilage is least affected, but as the bone is again approached the process is repeated, until between bone and cartilage there appears another mass of granulation tissue, which extends not only into the cartilage, but also into the bone. In the bone all the appearances are the same as those described in § 381. It must be remembered, too, that tubercle beginning in bone may give rise to tuberculous granulations under the cartilage, absorption of the cartilage, and ulceration into the joint, in which case there is also a form of white swelling. In both cases tuberculous granulations are found in the

tissues around the joint. Endarteritis obliterans (§ 273) is always a well-marked feature in these cases of synovial tuberculosis.

($\times 300$).—All the above appearances should be confirmed—the tubercle nodules in the swollen synovial membrane, the encroachment of the granulation tissue on the cartilage, the proliferation of the cartilage cells, and the gradual disappearance of the capsules and the matrix. The tubercle follicles are very well formed, the appearance of typical giant cells being very characteristic of this condition; the granulations in the rarefying bone, the points of commencing caseation and the proliferative changes in the cells of the intima of the vessels, are also well seen. In these tuberculous masses tubercle bacilli may sometimes be found. Examine a few of the muscle fibres from near the affected joint, and note that they are undergoing fatty degeneration, and that in some cases this is succeeded by great atrophy of the muscle.

In some forms of this disease it will be found that the cartilage cells, after proliferation, undergo rapid fatty degeneration, and then, along with the softened matrix, are absorbed (Billroth).

CHRONIC ARTICULAR RHEUMATISM, OR “ARTHRITIS DEFORMANS”

383. This condition, known also as rheumatic gout, is really a chronic inflammatory process. It is characterised by proliferation and destruction of the articular cartilages, thickening of the synovial membrane, sclerosis, eburnation of the bony articular surfaces, and formation of granulations which become cartilaginous, calcified, or even ossified.

Naked-eye appearances.—At the point where there is greatest friction the cartilage may have disappeared, and there remains simply an area of dense polished bone; around this a ring of cartilage is often present, the articular surface of which is peculiarly soft and velvety to the touch and in appearance; on examination with a magnifying glass this velvety appearance is seen to be due to the presence of a number of fine villous processes. In or under the synovial membrane, which is found only near the margins of the articular surface, small nodules, evidently the result of proliferation of the cartilage cells, are seen. These nodules in some cases are of considerable size, but later they disappear, and an ulcer is formed which gradually spreads. Around the joint itself, in the periosteum and tendons and in the synovial fringes, which are increased both in size and number, a

process of ossification is going on. In the later stages of the disease, the muscles, at first fatty, may become calcified: eventually the joint is surrounded by a number of characteristic smooth dense bony masses, partly formed as above, but partly the result of a pressing out of the soft granulation tissue from between the two articular surfaces, this soft tissue afterwards becoming first cartilaginous, and then ossified.

Prepare a piece of the cartilage from such a specimen (early stage)

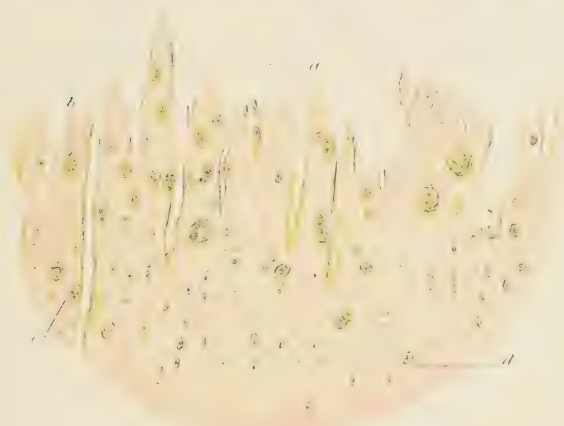


FIG. 193.—Section of ulcer of cartilage from a case of arthritis deformans. Stained with picro-carmine. ($\times 80$.)

- a.* Columns of cartilage cells, with accompanying matrix from between which some of the fibrillated matrix has been removed, after undergoing softening. (The velvet pile.)
- b.* Cartilage cells near the surface, fatty and granular.
- c.* Proliferating cartilage cells.
- d.* The deeper and more normal layer of cartilage.

(§ 60 or 63), stain (§§ 102, 103, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—At some parts there has been proliferation of the cartilage cells; those within an enlarged capsule are well formed and of considerable size, but those near the margin of the ulcer are extremely granular. Notice, too, that there is an entire absence in the floor of the ulcer of the horizontal layers of cartilage cells, which have apparently been removed by the rubbing together of the two rough

surfaces, the swollen cartilages in this process playing merely a passive part. Between the vertical rows of proliferating cells near the surface of the bone, the matrix is softened, and some of it has disappeared, and the villous processes, already seen with the hand-glass, can now be further examined. Near the margin of the ulcer the process of cell proliferation is more marked, but the horizontal rows are still seen. Observe the thickening of the synovial membrane and the formation of the small mass of vascular granulation tissue.

($\times 300$).—Granular cells, which are evidently fattily degenerated cartilage cells, are well seen; note the well-formed proliferated cells, and the splitting up of the cartilage into villous processes. The matrix between the rows of cells is seen to be finely fibrillated, the axis of fibrillation running down towards the bone. The villous layer consists simply of the deeper or vertical rows of cartilage cells, with a fibrillated matrix between. The bone beneath the cartilage, as well as that formed around the joint, is very dense and smooth; this is the result of a chronic osteitis.

In more *acute inflammation of cartilage*, the cells formed in the capsules are much more numerous, but are not nearly so large, whilst the matrix, after softening, may gradually disappear as the disease advances, and a mass of granulation tissue is left; suppuration may also occur.

GOUTY INFILTRATION OF JOINTS

384. This is an infiltration of the articular cartilages with urate of sodium chiefly, mixed with other urates, carbonates, and phosphates. These, when the infiltration is complete, form a chalk-like covering to the joint, or where the deposit takes place in the surrounding ligamentous and soft tissues, form chalk-like masses, which may even project through the skin. These latter, the so-called chalk-stones, by their presence may give rise to considerable inflammation, either of acute or of chronic form. On cutting into a gouty joint, soft chalky masses are first exposed, and the surfaces of the joint itself are found to be white, smooth or grooved, highly polished and chalky, from the rubbing together of the two infiltrated surfaces.

($\times 300$).—In the fresh condition (§§ 36 and 41), in a piece of the cartilage and in its underlying bone where the change is not far advanced, a number of acicular crystals may be seen arranged in stellate groups, the centre of each group being a cartilage capsule. The crystals are

so arranged around this that the whole mass presents the appearance of a thorn apple (Cornil and Ranvier). The distribution of the urates differs considerably in different cases, and it is held by some that the chalky deposits begin in the centre of the cartilage and then pass outwards, whilst others hold that they are most numerous

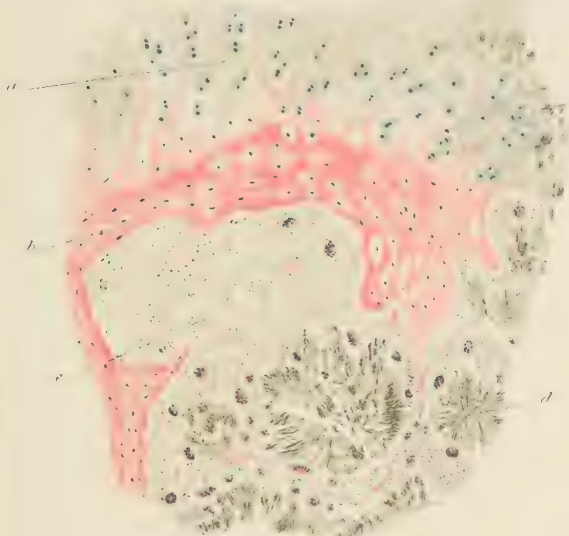


FIG. 194.—Section of articular cartilage with bone beneath from a gouty joint. Stained with methylene-blue and eosin. ($\times 50$.)

- a.* Layer of articular cartilage shading off into
- b.* Bony tissue.
- c.* Acicular crystals of urate of soda in the cartilaginous matrix.
- d.* Acicular crystals of urate of soda in the bony trabeculae and in the connective tissue of the bone marrow.
- e.* Normal bone marrow.

near the surface, and that they gradually spread downwards to the bone.

Here, as in most of the diseased conditions of cartilage already examined, the altered cartilage plays a comparatively passive part. As the infiltration which follows inflammation or depression of the cartilaginous tissue takes place, the mass is rubbed down by simple

friction, as in fatty degeneration of the cartilage cells, where the cartilage matrix is softened or becomes fibrillated, and is worn away ; or in acute inflammation of cartilage, where the cells proliferate, the matrix softens, becomes mucoid, and is removed, and the cartilage disappears. The more active the proliferation of the cells, the greater is the divergence from the appearances presented by the ordinary type of cartilage.

TUMOURS OF BONE AND JOINTS

385. The principal tumours of bone are *exostoses*, *osteoid chondroma*,

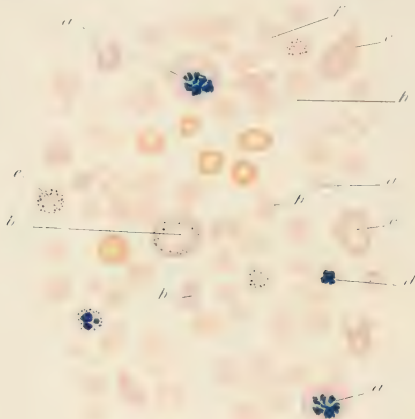


FIG. 195.—Blood film from a case of pernicious anemia. Stained by Jenner's method. ($\times 600$.)

- a. Megaloblasts with lobulated nuclear chromatin.
- b. Megaloblasts with granules of chromatin distributed through the cytoplasm.
- c. Megalocytes.
- d. Normoblast with lobulated nuclear chromatin.
- e. Normoblast with granules of chromatin scattered through the cytoplasm.
- f. Normal blood cells.
- g. Microcytes.
- h. Poikilocytes.

fibroma, *myxoma*, *cystic tumours*, especially in the jaws; *sarcomas* of various forms, more especially the myeloid or giant-celled sarcoma

and the mixed sarcoma found in the lower jaw, as one of the most frequent forms of malignant epulis; osteoid and osteo-sarcoma. *Primary cancer* is comparatively rare, but *secondary cancer* and *secondary epithelioma* are frequently met with, when they grow at the expense of the bone substance proper; the bone eventually becoming very brittle or fragile.

Primary malignant tumours growing in connection with joints are very few in number, though secondary tumours, extending from bone or from the surrounding soft tissues, are by no means uncommon.

Of the primary simple tumours the most common are *ecchondroses*, which are found growing principally in the intervertebral discs; *fibromas* forming the so-called loose cartilages of joints (especially in the knee); and *lipomas*, rarely met with as arborescent growths from the fatty synovial fringes. (See Chapter XIV.)

EXAMINATION OF BLOOD AND BONE MARROW

386. To compare the cells met with in normal blood with those met with in disease is a somewhat difficult matter, but whilst the student is referred to special treatises on the blood for a systematic account of the examination of the blood, it seems to be advisable to describe some of the abnormal cells met with (*a*) in pernicious anæmia, (*b*) in chronic myelogenous leukæmia, and (*c*) in chronic lymphatic leukæmia, in order that when he comes to the detailed examination of the blood he may be able to recognise these various cells. The student should make himself thoroughly familiar with the appearances of both normal and abnormal cells of the blood before he undertakes a systematic examination in the ward.

The first two of these, (*a*) and (*b*), are invariably associated with distinct changes in the bone marrow, especially in the shaft of the long bones, and may therefore appropriately be introduced at this point, whilst even in the third form (*c*) there is usually a considerable increase in the amount of lymphoid tissue present in the marrow within the shafts of the long bones.

PERNICIOUS ANÆMIA

387. Take a drop of blood from the lobe of the ear or from the side of the finger-nail; do not exert any pressure, but make a puncture

deep enough to allow sufficient blood to come freely and regularly. Make a film (§§ 152 and 171). Do not use the "cigarette paper" or the "scrape" method, or all the large cells will be drawn to

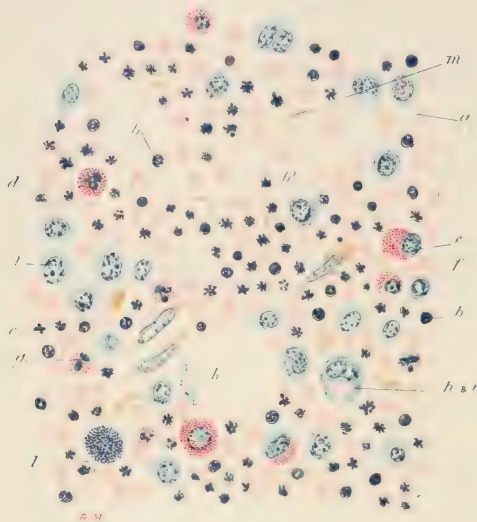


FIG. 196.—Section of bone marrow (from the femur) from a case of pernicious anemia. Stained with methyl-blue and eosin. ($\times 600$.)

- a. Red blood corpuscles.
- b, b'. Normoblasts with round and lobed nuclei within blood vessel (? megaloblasts).
- c. Similar cells around a blood vessel.
- d. Coarsely granular eosinophile cell.
- e. Coarsely granular eosinophile myelocyte.
- f. Finely granular neutrophile myelocyte.
- g. Polymorpho-nuclear leucocyte.
- h. Large mononuclear phagocyte.
- i. Macrophage containing ingested red blood corpuscle.
- j. Hyaline myelocyte.
- k. Endothelium of blood vessel.
- l. Basophile cell (? myelocytes).
- m. Blood pigment (spodogenous iron) deposited in the bone marrow.

one end of the slide, and it will be difficult to make anything like an accurate differential count. The blood is pale, watery, and coagulates slowly. Fix the film (§ 59) and stain (§ 151). Although

a low power ($\times 50$) and then a higher power ($\times 300$) may be used for the examination of the blood in order to get a rough determination of the number and character of the cells present and to see that no rouleaux are formed, it is well to carry out the greater part of the examination under a still higher power ($\times 600$). In spite of the watery character of the blood, most of the individual red corpuscles evidently contain the normal amount of hæmoglobin, *i.e.* they take on a deep eosin tinge, though some contain much more than others, this factor, "hæmoglobin value," varying considerably more than in normal blood. On the other hand, there is usually a very great diminution in the number of these corpuscles; they may be only one-fifth or one-tenth of the normal number. Poikilocytes or distorted corpuscles are fairly numerous, normoblasts or nucleated red blood corpuscles and microblasts (small nucleated red corpuscles) are present, and, especially in the advanced stages of the disease, megaloblasts—large nucleated red cells, and giant red corpuscles $15-18\mu$ in diameter, are numerous. This last type of cell is apparently confined almost entirely to pernicious anæmia, in which there appears to be some special stimulation of the bone marrow. Certain of the red cells are stained more or less uniformly by methylene-blue (polychromatophilia is often found), whilst in others strongly basophile granules are present, sometimes in large numbers. The number of polymorpho-nuclear leucocytes is, if anything, diminished, especially in the later stages of the disease, but the lymphocytes are usually increased in number. Blood platelets (§ 217) are, as a rule, fewer than in normal blood.

On examining a vertical section through one of the long bones it will be noted that the red colour of the marrow of the expanded ends of the bone is more marked than usual, whilst in the shaft, in place of the yellow fatty marrow seen in the normal bone, is a soft, deep red, gelatinous mass, which has been compared to blood-clot or again to red currant jelly. A somewhat similar marrow is seen in the bones of patients who have succumbed during the course of a secondary anæmia, but it is seldom quite so pronouncedly "blood-clot-like" as in the pernicious form, where it is vascular, soft, and readily scooped out from its position. The spaces that it fills seem to be larger than in the normal bone, as though in addition to the displacement of the fatty marrow there had been some absorption of the bony walls of the cavities by this soft, cellular mass.

In making a naked-eye examination of the bone marrow it should be remembered that the age of the patient from whom it comes should always be taken into account. In the child the normal marrow, especially in the shafts of the long bones, is much redder than it is in the adult, in whom only the portion of marrow contained within the ends is red; this being sufficient to keep up a supply of red blood corpuscles to make good the normal waste. During senescence the marrow gradually loses its fatty character in the shafts, and even its red character in the short bones and at the ends of the long bones, becoming gelatinous in appearance and less active as regards the production of both leucocytes or red blood corpuscles.

Harden (§ 58, 61, or 63), cut (§ 92), stain (§§ 110 (*b*), 149, or 115 and 132), and mount (§§ 193 and 199).

($\times 50$).—The marrow is at once seen to be very different from the ordinary fatty marrow. The fat cells have almost disappeared, and in their place is an exceedingly cellular mass perforated by a regular network of blood vessels, which latter appear to converge to or radiate from the centre of the shaft. The blood vessels are lined by endothelial cells. It is evident even under this power that the cells of which the marrow appears to be made up vary greatly in size and structure. These cells, however, are best seen under the high power, under which they may be examined at once.

($\times 600$).—The blood vessels with their endothelial lining are readily distinguished. Within them red blood corpuscles, nucleated and non-nucleated, large, small, and irregular, and a number of leucocytes and lymphocytes may usually be seen. In spaces or sinuses outside these vessels, cells of various kinds are present in enormous numbers. It is the character and proportion of these cells that give the special features to the bone marrow of pernicious anæmia. In addition to the endothelial cells of the blood vessels a series of spindle-shaped sections of cells may be seen lying on very delicate connective tissue trabeculae. These cells and trabeculae are of interest because in and on them may often be seen granules of altered blood pigment which give the Prussian-blue iron reaction (§ 249)—spodogenous iron. This corresponds to the iron found in Kupffer's stellate cells in the liver and in the endothelial cells of the spleen in this same disease, and as its name indicates is probably derived from broken-down red blood corpuscles. Lying between these strands in vascular sinuses, as it were, are red cells in all stages of development—normo-

blasts with rounded and lobed nuclei, these latter deeply stained with methylene-blue, microblasts and megaloblasts with similar nuclei. There are also normal blood corpuscles, but these are proportionately few in number. Macrocytes are present but not in such large proportions as are the large nucleated forms. Around or in the outer portion of the walls of these vascular spaces and channels, hyaline cells with rounded and elongated vesicular nuclei—hyaline myelocytes—are far more numerous than in normal bone marrow. Some of them are distinctly phagocytic and have taken red blood corpuscles into their substance. Transitional cells from this form to the neutrophile polymorpho-nuclear myelocyte, eosinophile and basophile myelocytes, from which normally are developed the corresponding leucocytes, and fairly fully developed eosinophile leucocytes and neutrophile polymorpho-nuclear leucocytes are all met with in the same position. We thus have an exceedingly characteristic picture, which should be studied most carefully.

It is assumed that in pernicious anæmia there is great destruction of red blood corpuscles. (Hunter maintains that this goes on in the portal system, especially in the spleen, and is the result of the action of destructive poisons formed in the alimentary canal.) The bone marrow is constantly engaged in an attempt to make good this loss, utilising much of the iron that is set free from the broken-down erythrocytes. At first the reproduction of corpuscles, both red and white, goes on in the ordinary fashion, but after a time the normal process is unequal to the demands made upon it, and the embryonic method of blood formation is again brought into play. Here there is a marked increase in the number of megaloblasts and macrocytes formed. Microcytes and microblasts are present in fair numbers, but the normoblasts and normal erythrocytes are comparatively few in number. The altered (exhausted) bone marrow which in the earlier stages of the process may form an increased number of granular leucocytes of various forms, has lost its power of producing the normal number of these leucocytes—*i.e.* its altered power of forming normal red blood corpuscles is accompanied by a diminished capacity to manufacture white blood corpuscles of various types. This alteration in the structure and function of the bone marrow may of course be due to some special stimulation, whether by products of disintegration of the red blood corpuscles, by the poisons formed in the alimentary canal, or by some special or specific virus, is not yet determined. In blood

and bone marrow that has been kept for a time Charcot's crystals, octahedral or acicular crystals, are found free in the serum and in the polymorpho-nuclear and eosinophile cells. They are seldom or never found in perfectly fresh blood.

In some cases of pernicious anæmia there is an increase in the amount of lymphatic tissue in the bone marrow, this apparently being the result of a reaction of the lymphoid tissue to the special stimulation. Hence the increase in the number of lymphocytes in the blood which is sometimes observed in this condition.

MYELOGENOUS LEUKÆMIA OR LEUCOCYTHÆMIA

388. The blood from a case of myelogenous leukæmia flows slowly, has a peculiar light red colour, is milky or greasy-looking and turbid as though containing fatty matter; it clots imperfectly, and the clot is much paler and less consistent than normal.

Spread (§ 171), fix (§ 59), stain (§§ 148 and 151), and mount (§ 199).

($\times 50$).—There is a great increase in the number of white cells both relatively and absolutely. The red blood corpuscles are often greatly diminished in number, in some cases falling as low as one million per cubic millimetre. In very advanced cases the white cells may be almost as numerous as the red cells.

($\times 600$).—Polymorpho-nuclear leucocytes and myelocytes, which latter resemble the large lymphocytes and hyaline cells of normal blood except that they are larger and have a vesicular nucleus, are much increased in number. This nucleus stains comparatively lightly with methylene-blue; the protoplasm in a few cases is hyaline, but it usually contains neutrophile finely granular myelocytes. These finely granular myelocytes in all stages of development, from large, almost non-amœboid cells with their rounded vesicular nuclei up to the almost fully developed polymorpho-nuclear cell, are specially numerous. Eosinophile and basophile myelocytes and leucocytes are also increased in numbers. The "mast cells," which may be fairly numerous in very chronic cases, and their granules are not so distinctly meta-chromatic, as are those of the mast cells found in the normal tissues. Polymorpho-nuclear basophile cells are much more frequently met with than are the basophile myelocytes. Mitotic figures may rarely be seen in the leucocytes and in the nucleated red blood corpuscles which are present in considerable numbers. These granular cells of

various form are very characteristic of myelogenous leukæmia. The

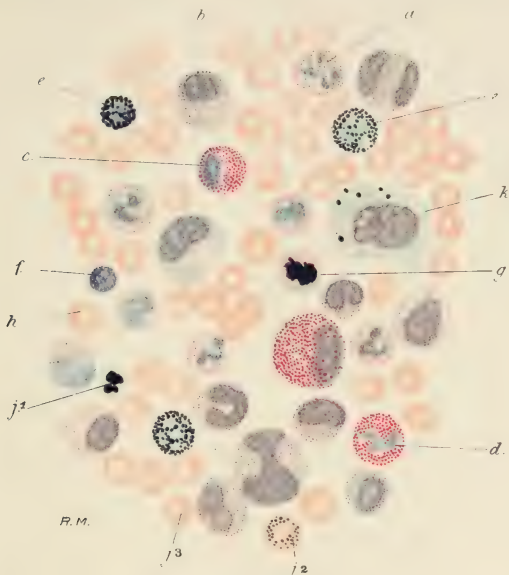


FIG. 197.—Blood film from a case of myelogenous leukæmia. Stained by Leishman's method. ($\times 600$.)

- a. Finely granular neutrophile or faintly oxyphile polymorphonuclear cell.
- b. Immature finely granular cell from which the above is derived. The finely granular myelocyte is not found in normal blood, but is numerous in the bone marrow. Single and divided nuclei.
- c. Coarsely granular oxyphile myelocyte; the form of immature cell of this type usually found in the bone marrow.
- d. Coarsely granular leucocyte.
- e. Basophile cells.
- f. Lymphocyte.
- g. Megaloblast with lobulated nucleus and showing polychromatophilia.
- h. Normal hæmatocytes.
- j¹. Normoblasts with dividing nucleus, j². with fragments of nuclear chromatin substance distributed through the cytoplasm. j³. with similar chromatin granules only.
- k. Large mononuclear cell. Hyaloblast.

number of lymphocytes does not appear to be increased—in fact, in

certain cases they appear to be diminished in number, relatively if not actually. This applies also to the hyaline leucocytes and myelocytes.

The bone marrow from such a case is usually light red or pink in colour and firm in consistence, often extending from the extremities into the shafts. In some cases the whole marrow is affected, but in others only irregularly scattered patches may assume these characters, the pink patches often being mottled with grey or greyish-yellow as the case may be, whilst small hæmorrhages are of frequent occurrence. The bony trabeculæ are thinner and more brittle, and the marrow spaces appear to be increased in size, *i.e.* there is more marrow and less bone, but the red marrow appears to extend chiefly at the expense of the yellow or fatty marrow, which is absorbed as the former increases in amount.

Harden in formol alcohol (absolute alcohol containing 10 per cent. of formalin) cut (§§ 91 and 92), stain (§§ 148 and 151), and mount (§§ 193 and 199).

($\times 50$).—The section appears to be much more cellular than normal, the blood channels may be narrow, a large accumulation of red blood corpuscles lining the vessels and sinuses, whilst outside them nucleated leucocytes are usually present in considerable numbers, this great increase being in the number of myelocytes.

A few adipose cells may be seen here and there, but the yellow marrow structure is almost lost. Small collections of lymphoid tissue may also be seen.

($\times 600$).—In the reticulum of the bone marrow from a case of myelogenous leukæmia the formation of the red cells by rapid proliferation in the immediate neighbourhood of the circulating blood can be readily made out. Nucleated red blood corpuscles, layer upon layer, sometimes causing narrowing of the lumen of the vessel, are seen in great numbers. Many of the red corpuscles are distinctly nucleated, and mitotic figures may sometimes be seen in them, whilst here and there distinct polychromatophilia may be seen in certain of them. Outside the blood vessels or away from the blood stream myelocytes in great numbers are to be found. Most of these, which appear to be in the reticular tissue, have a vesicular nucleus staining somewhat lightly, and their protoplasm is "peppered" with neutrophile granules, though basophile and eosinophile granules may be found in a certain proportion of the cells. Mitotic figures may also be seen.

A few large hyaline cells may be seen. In a few instances the myelocytes appear to be undergoing fatty degenerative changes, and in most cases they are less actively amoeboid than in normal marrow. This great increase in the number of characteristic white cells distinguishes the marrow of a case of myelogenous leukæmia from that found in the anæmias and in lymphatic leukæmia. The lymphocytes found in the bone marrow in such cases are probably developed from the lymphoid tissue, which is always found in this position. Charcot's octahedral crystals may be found within the polymorpho-nuclear and eosinophile cells in this marrow, especially when, as in the case of blood from such a source, it has been kept for a time. In smear preparations of the bone marrow hardened as above and stained (§ 148 or 151), examined under the high power, all the above cells may be very readily demonstrated.

LYMPHATIC LEUKÆMIA

389. Lymphatic leukæmia, which is marked by great proliferation of the lymphoid tissue and an enormous increase of the various forms of lymphocytes in the blood, may occur in either an acute or a chronic form. In the acute form, in which the spleen is not much enlarged, we have a very marked increase in the number of lymphocytes, both large and small, in the blood, these sometimes constituting as many as 90 per cent. of all the white cells present. The disease runs a rapid course, and associated with it is a great tendency to hæmorrhage into the mucous, serous, and cutaneous membranes, the brain, and the tissues of other organs. In the chronic form the spleen is usually enormously enlarged (§ 350). The increase in the number of lymphocytes in the blood is very marked, and there is usually a considerable degree of anæmia. Here also the blood is pale and creamy looking and somewhat turbid. In both of these forms there seems to be a proliferation of the lymphoid tissue and of the endothelial cells lining the sinuses of the spleen. The bone marrow, however, appears to be little affected except that there is an increase in the amount of lymphoid tissue, which may so encroach upon the leucoblastic and erythroblastic tissue that the granular cells and red blood corpuscles are actually produced in smaller numbers. A number of nucleated red blood corpuscles make their appearance in the blood during the course of this disease, and

polychromatic staining of the red cells, indicating a degeneration, may also be met with. The amount of hæmoglobin is low.

($\times 800$).—The lymphocytes, especially those of the smaller form, are considerably increased in number, nucleated and degenerated

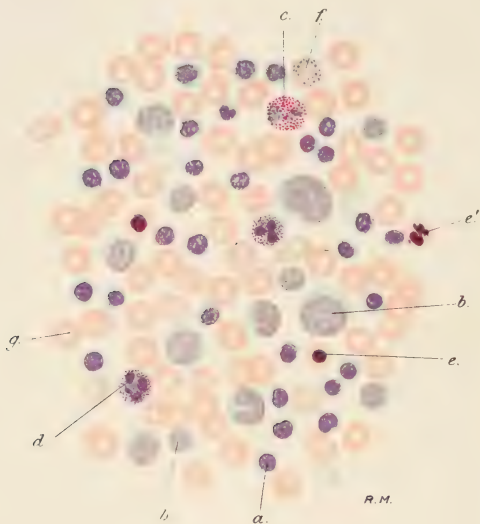


FIG. 198.—Blood from a case of chronic lymphatic leukaemia. Stained by Leishman's method. ($\times 600$.)

- a.* Lymphocytes, greatly increased in number.
- b.* Hyaline myelocytes.
- c.* Coarsely granular oxyphile leucocyte.
- d.* Finely granular polymorpho-nuclear cells.
- e.* Normoblasts or nucleated red cells (*e'*) with dividing nucleus.
- f.* Normoblast with basophile staining points (degenerative?) distributed through the cytoplasm.
- g.* Normal red blood corpuscles.

blood corpuscles are numerous in comparison with the number of erythroblasts. Polymorpho-nuclear leucocytes and eosinophile cells may be met with, but seldom in increased number, and sometimes they may be actually fewer than normal.

MARROW FROM A CASE OF ACUTE PNEUMONIA

390. During the course of certain specific fevers, of suppuration, and under the stimulation of certain toxins, the bone marrow appears to become excessively active and to form an increased number of leucocytes. As during these fevers there is frequently a great

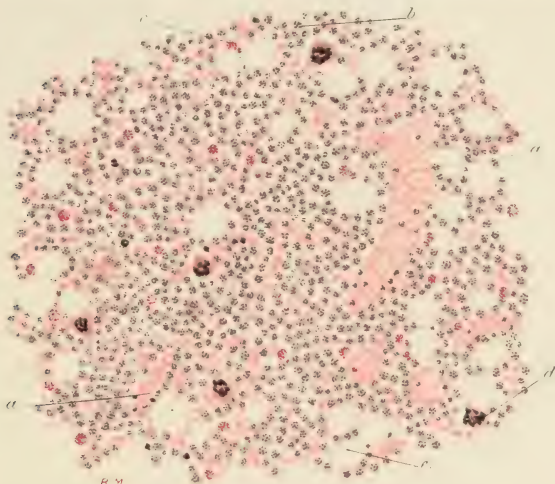


FIG. 199.—Section of bone marrow taken from the rib from a case of pneumonia. Stained with hæmatein and eosin. ($\times 120$.)

Here there is a marked leucoblastic condition.

- a. Red blood corpuscles within and outside the vascular channels.
- b. Polymorpho-nuclear leucocytes and myelocytes.
- c. Coarsely granular eosinophile cells, leucocytes and myelocytes.
- d. Myeloid or giant marrow cells.
- e. Fat spaces.

destruction of red blood corpuscles, we have associated with this proliferation of the leucocytes an increased erythroblastic action of the marrow. Hence very marked changes in the bone marrow. Under this pathological irritation, as in the case of an acute lobar pneumonia, the bone marrow reacts by producing an increased number of normal leucocytes which, making their way into the circulating

blood, give rise to the condition known as leucocytosis. Fix (§ 59 or 61), stain (§§ 115, 132), and mount (§§ 193 and 199).

($\times 120$).—Examine a section of the hyperæmic bone marrow

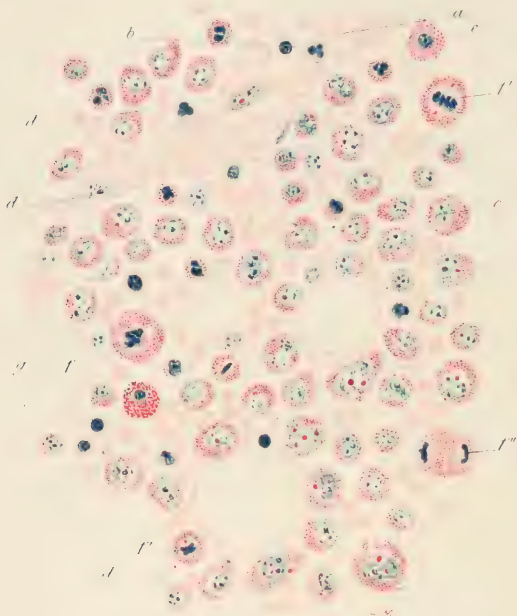


FIG. 200.—Section of the bone marrow from a case of pneumonia. Neutrophile leucoblastic marrow. Stained with methylene-blue and eosin. ($\times 600$.)

- a.* Red blood corpuscles.
- b.* Polymorpho-nuclear leucocyte.
- c.* Finely granular myelocyte.
- d.* Endothelial cell of blood vessel.
- e.* Coarsely granular eosinophile myelocyte.
- ff. f''.* Various stages of mitotic division of the finely granular myelocyte.
- g.* Nucleated red blood corpuscles. Normoblasts.

from such a case. Here there is an enormous increase in the cells occupying the reticulum between the delicate blood vessels of this tissue. These cells *in situ* are seen to be of the myelocyte form, with

somewhat rounded or oval nuclei and hyaline protoplasm or protoplasm in which are neutrophile or eosinophile granules, the former predominating very largely. A few cells with basophile granules and large multinucleated giant cells may sometimes be seen. Making their way into the vessels the myelocytes appear to assume the polymorpho-nuclear form as soon as, or even just before, they reach the blood vessels, but the actual polymorpho-nuclear leucocytes form a comparatively small proportion of the cells in the marrow network. It will be noted that the bulk of these cells are stored up outside the blood vessel, but that they can readily make their way into the vascular channels, apparently as the result of chemiotactic attraction.

($\times 600$).—Many of these cells are seen to be undergoing mitotic division, beautiful examples of which may be seen in the drawing. The myelocytes, neutrophile and eosinophile, with their rounded vesicular nuclei, may also be seen being transformed into polymorpho-nuclear and eosinophile leucocytes. The non-nucleated red blood corpuscles are relatively few in number, and they, with a number of nucleated corpuscles, are seen to be lying either in the blood vessels or sinuses or in immediate relation to their walls. Hyaline cells are comparatively few in number, and lymphocytes, or any cells resembling them, are exceedingly rarely met with except in the lymphoid tissue of the bone. As a result of this stimulation of the bone marrow and the great increase in the number of myelocytes, there seems to be an increased store of cells on which a draft may be made for the production of polymorpho-nuclear leucocytes.

391. From the examination of these various specimens it will be seen that the bone marrow, stimulated or exhausted, as the case may be, has its function increased or diminished, so that it is able to produce an increased or diminished number of red cells and an increased or diminished number of white cells. In certain cases where there is special stimulation of the lymphoid tissue, this tissue may become so active and exuberant in its growth that it may "replace," partially or almost completely, the normal leucoblastic and erythroblastic marrow tissue.

CHAPTER XII

NERVOUS SYSTEM

TUBERCULOUS MENINGITIS—ACUTE HYDROCEPHALUS

392. Tuberculous meningitis, or inflammation of the pia mater, due to tuberculous deposit in the sheaths of the small vessels which ramify in it, is very frequently the cause of death of children in whom there is general tuberculosis.

Naked-eye appearances.—The surface of the membrane is congested; beneath it there is considerable flattening of the convolutions, owing to the distension of the ventricles, in consequence of which, too, the whole upper surface of the brain has a peculiar dry appearance, the fluid having been squeezed from the subarachnoid space. At the base of the brain, and extending along the fissures of Sylvius and Rolando, along the superior crura cerebelli, and between the occipital lobes, the inflammatory process with its accompaniment of tubercle can be well made out. In these positions the various soft structures are matted together by a slightly opaque yellowish lymph; when this is torn away, a quantity of turbid fluid, in which flakes of lymph are floating, exudes from the subarachnoid space. A similar fluid may also be found distending the ventricular cavities, the distension being especially well seen in the lateral ventricles. This is due to the interference with the flow of lymph; there is often, also, an enormous accumulation of fluid at the base of the brain. This leads to flattening of the convolutions and compression of the brain substance. The accumulation takes place so rapidly that the pressure can exert little influence on the bones of the cranium. In consequence of this accumulation of fluid the condition is known as acute hydrocephalus. In most cases, on separating the parts at the base of the brain, small grey or white tubercle nodules may be seen to stand out prominently from the injected pia mater. The pia mater is

seen to be thickened between the tuberculous points ; it is somewhat cloudy, and is covered by a thin yellowish, almost purulent, layer. Around the blood vessels there is the same peculiar opacity, which, as will afterwards be found, is due to a small cell infiltration into the sheath of the vessel.

"To find tubercle, the pia mater should be removed from those regions where it is most frequently found, such as the fissure of Sylvius and the superior crura cerebelli. The piece of the membrane should then be agitated in water till the adhering fragments of cerebral tissue are separated, and, on holding it up to the light, small whitish spots will be seen in the membrane. This examination must not, however, be considered sufficient. The pia mater should be carefully spread upon a glass slide, when, with a low power, granulations will be perceived which were not before recognisable with the naked eye" (Cornil and Ranvier).

Harden a piece of the pia mater, with a piece of the brain tissue attached (§§ 57 (*a*) and 62 or 63), stain (§§ 102 or 104, 110 (*b*), 132, and 183), and mount (§§ 193 and 199).

($\times 50$).—Note first the general proliferation of cells, especially around the blood vessels, and then the tuberculous granulations which are situated, most frequently, near the points of bifurcation of the vessels, or at irregular intervals along the course of the smaller vessels. Each of these tuberculous masses consists of cells, varying very greatly in size and shape. They accumulate around the vessel and distend the perivascular sheath. The vessel itself is frequently blocked by a coagulum at the point of swelling, and a peculiar process of endarteritis with a form of giant cell formation may often be seen. Marked proliferation of the endothelial cells lining the arachnoid spaces may be made out even under this power. Typical tubercle follicles (see § 246) with caseous centres, and in some cases well-defined giant cells, are seen, especially where the process is running a somewhat less acute course.

($\times 300$).—The large endothelioid cells in the perivascular sheath and in the meshes of the arachnoid membrane vary in shape, and contain from one to four or more nuclei. Along with them are numerous small round cells, each containing a single nucleus. The reticular formation varies in different cases ; in acute cases being almost wanting, in less acute forms being present. The same holds good of the giant cells. Note that the proliferating cells are derived from the endo-

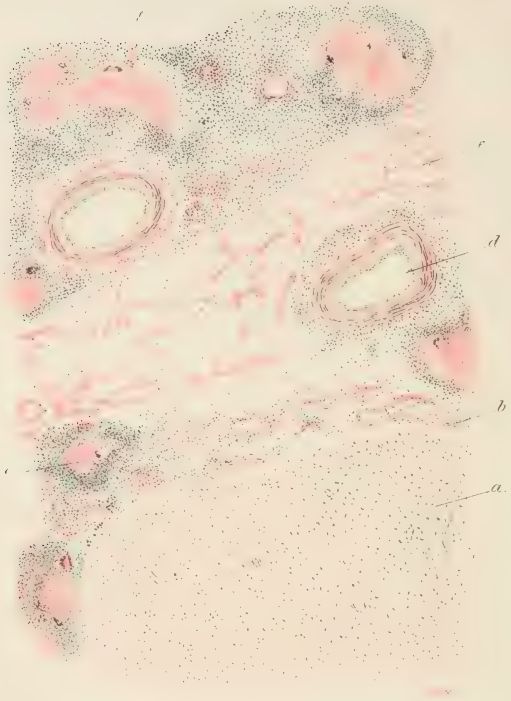


FIG. 201.—Section of the surface of the cerebral cortex and the pia arachnoid membranes from a case of tuberculous meningitis. Stained with logwood and eosin. ($\times 50$.)

- a.* Cerebral cortex in which are seen numerous vessels (normal).
- b.* Vascular pia mater.
- c.* Tubercle nodule composed of several follicles caseating in the centre or with giant cells; epithelial cells and small round cells well seen.
- d.* Large vessel, surrounded by larger number of leucocytes, running in the pia arachnoid.
- e.* Fibrinous lymph lying in network of the arachnoid membrane.
- f.* Caseating tuberculous nodules surrounded by proliferating endothelial cells, leucocytes, and lymphocytes.

helium lining (*a*) the perivascular lymph spaces, (*b*) the spaces in the pia arachnoid, and (*c*) the fibroblasts or connective tissue cells. The small round cells are (*a*) leucocytes and (*b*) lymphocytes.

A chronic form of tubercle, which does not usually give rise to acute hydrocephalus, is sometimes found in the substance of the brain, but much more frequently in the cerebellum. It appears to begin in connection with the pia mater, from which it extends rapidly into the substance of the brain. A typical mass in the cerebellum may be an inch or more in diameter; it projects from the surface, and also passes for a considerable distance into the grey matter; it is firm to the touch, and somewhat tough. On section the outlines are seen to be irregular and sinuous or lobulated, as though several tuberculous masses had become fused; the centre of the mass is cheesy, and may be readily broken down with the fingers, but around the centre is a grey gelatinous zone, which gradually merges into the surrounding nerve tissue.

Harden (§ 62 or 63), stain (§§ 102, 104, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—Observe the typical caseous material in the centre of a well-formed tuberculous growth, often with well-developed giant cell systems, extending outwards in all directions. The tissue surrounding the tuberculous mass is distinctly fibro-cellular, and there is a marked increase of the neuroglia cells. In the sheaths of the blood vessels there is a process similar to that already described as occurring in acute tuberculosis, the infiltration of the perivascular sheath with small cells and obliteration of the lumen of the vessel being specially prominent features. Tubercle bacilli may also be demonstrated in these perivascular tubercles.

($\times 300$).—Verify these appearances.

GUMMATA OF THE BRAIN AND ITS MEMBRANES

393. In tertiary syphilis, inflammatory gummatous patches involving the membranes and the cerebral cortex, especially near the base of the brain in the interpeduncular space, are frequently met with.

Naked-eye appearances. Where the process is well advanced, there may be single or multiple growths appearing first in the membranes, in the larger sulci or spaces, or gradually invading the subjacent cortex. These growths are surrounded by a firm fibrous capsule, bands from which run for short distances into the surrounding brain substance,

which is usually somewhat firmer than normal. Within this fibrous capsule is a zone of pinkish gelatinous-looking tissue, pinker at the margin, but grey or yellowish-grey nearer the centre, where it gradually merges into yellow caseous points or patches. In all cases the pia mater is bound down to the cortex.

Harden (§ 58, 60, or 63) and stain (§§ 102, 104, or 110 (*b*), and 132).

($\times 25$).—It is seen at once that the process extends along the course of the vessels which, after ramifying in the pia mater, run into the cortex. The pia mater is greatly thickened, and around each artery and vein accumulations of small round cells may be seen. The intima of the larger arteries is usually thickened by proliferation of its cells. Similar changes may be seen around the vessels in the cortex. The gelatinous zone is now seen to be made up of small masses of granulation tissue composed of nucleated cells. Where these masses of cells are undergoing degeneration they become first hyaline, then granular, and ultimately leave nothing but a mass of granular débris corresponding to the yellow caseous points and masses. The fibrous-looking capsule still contains numerous cells, except in very old gummata, where it consists simply of well-formed fibrous tissue. Shooting out from the gumma are numerous small vessels, each surrounded by numbers of small cells similar to those above described.

($\times 300$).—Confirm the above appearances. Note that the cells around the vessels are usually situated in the perivascular spaces, that, although many of them are small cells each with a single nucleus, there are also large endothelioid cells, often containing several nuclei. The changes in the vessels are specially well marked in the brain. The proliferation of the intimal cells, atrophy of the muscle fibre of the middle coat, with increase of the cellular elements and proliferation of the cells in the adventitia, are all well-marked features. The gradual cutting off of the blood supply, the hyaline and then fatty and granular degeneration of the new masses of cellular tissue, or their conversion into fibrous tissue, are well seen. Around the gumma, especially near the vessels with their infiltrated walls, the brain substance is undergoing degenerative and atrophic changes.

CEREBRAL HÆMORRHAGES

394. Fresh hæmorrhages, the result of increased pressure within arteries the walls of which have undergone fatty degeneration or fibroid

thickening, especially of the muscular coat (if present) and of the adventitia, are frequently met with; similar hæmorrhages may also result from the rupture of a single aneurism of a larger vessel, or of a group of miliary dilatations, which may be readily recognised by the ragged walls, and the dilatations on the vessels in the immediate neighbourhood of the clot (§ 276). Hæmorrhages occur most frequently in the corpus striatum, optic thalamus, and internal capsule; more rarely in the white substance of the convolutions; and least frequently in the pia mater, cerebellum, pons varolii, and medulla oblongata.

To examine the vessels around a hæmorrhagic focus, the result of rupture of miliary aneurisms, open into it and cut it away with the surrounding brain tissue. Carefully macerate the whole in water, changing every three or four days, until the brain substance is soft enough to be easily removed by a small jet of water (see also § 275). When the vessels are thoroughly cleansed, they may be spread out on a glass slide and examined.

Harden a small piece of the perfectly fresh brain tissue, taken from near the hæmorrhage, with its altered vessels (§§ 59 and 62 or 63), and stain (§§ 102, 110 (*b*), and 132). Another piece should be hardened entirely in methylated spirit (§ 60), to do away with any chance of the chrome colouring matter from the Müller's fluid being mistaken for altered pigment.

When a large amount of blood has been effused, it is first broken down and absorbed, as is a clot in any other part of the body; but changes are also set up in the surrounding tissue which result in the formation of either a cyst or a cicatrix. When a cyst is formed the walls are tough and fibrous, owing to the setting up of chronic inflammatory or irritative changes, the solid constituents of the clot have all been removed, and there remains a more or less clear fluid with a yellowish tinge. In the immediate neighbourhood of the fibrous wall there is a peculiar yellow opaque tissue, the result of the deposition of altered blood pigment in the lymphatics and cells of the altered brain tissue.

Examine small scrapings from the inner wall ($\times 600$), and observe that there are numerous small round cells which contain crystals in the form of rhombic plates or needles, evidently hæmatoidin crystals derived from altered blood pigment. Similar larger free crystals may be seen, and also a number of granular cells (compound granular corpuscles),

the granules in which stain black with osmic acid (§ 135). A number of fat globules are also usually met with in this position.

If a thin section of the wall be examined unstained, it will be found to consist in great part of neuroglia cells, the processes of which are closely matted together, with here and there a few altered nerve fibres, many of which are varicose and fatty. Between these are crystals or granules of altered blood pigment. The crystals are especially numerous in the opaque yellow zone surrounding the capsule, where also the



FIG. 202.—Drawing of connective tissue, etc., of medulla oblongata in a case of chronic inflammation, to show the Deiters' cells. Stained with carmine and half-cleared up. ($\times 800$.)

- a.* Connective tissue nuclei, around which there is as yet no formed material. Contractile nucleus well marked.
- b.* Nucleus of endothelial lining of wall of
- c.* Capillary vessel.
- d.d'.* Connective tissue corpuscles in different stages of development (Deiters' cells). Note the branching processes.
- e.* Nerve cells with pigmented nuclei. Each contains a nucleolus.
- f.* Young (*c.t.*) nuclei or leucocytes lying in lymph space.

fatty granules are more numerous. In the sheaths of the vessels fatty granules and altered coloured and colourless blood corpuscles are found, whilst in the larger cells lining the lymph spaces, or more frequently lying free in them, blood crystals may be seen. In a cyst formed as the result of an embolic softening few or no blood crystals are found in the walls of the sacs, as there has been *no great escape of blood from the vessels*.

In embolic softening there is simply fatty degeneration of the tissues ; and a mass of granular debris and fat crystals is all that is found under the microscope, save that there may be an increase in the number of leucocytes, along with other evidences of slight inflammatory changes around the vessel. Where the softened area is due to thrombosis, in which the cutting off of the blood supply is gradual, there is true fatty degeneration or yellow softening. The so-called red softening of the brain appears to be an inflammatory process leading to fatty degeneration, in which there is very marked congestion of the vessels. In such a condition note the proliferation of the neuroglia cells, the exudation of leucocytes, and the hæmorrhages into the perivascular sheath. In connection with the various degenerative changes which occur, the amount of blood in the part, the amount of infiltration with leucocytes, and the extent and rapidity of the fatty change in the nerve fibres and connective tissue cells, must all be remembered when an attempt is made to explain the causes of the yellow or the red forms of cerebral softening. The cicatrix left is made up of fibrous tissue or condensed neuroglia. Its structure is very readily made out.

Another section of the wall of the cyst may be stained with carmine (§ 106), but, instead of being completely cleared up, it should be treated with methylated spirit (instead of absolute alcohol), and left in this long enough for part only of the water to be driven out ; partially clear in clove oil, mount in dammar mounting fluid, and examine at once, as preparations made in this way do not retain their characteristic appearances for long. Such a method is especially useful for demonstrating neuroglia cells with their delicate branching processes.

OTHER PATHOLOGICAL CONDITIONS

395. Of the other pathological conditions met with in the brain may be mentioned the various inflammatory changes in the membranes ; these, making allowances for the different structures affected, correspond with those set up by inflammation in other positions. There is distension of the vessels, migration of leucocytes, and exudation of fluid into the perivascular lymph spaces, proliferation of connective tissue cells, and a gradual formation of new fibrous tissue. We also find pigmentation and small hæmorrhages. In the brain substance beneath, either in the cortex or in the ventricles, there is also evidence of inflammation ; one of the most marked of these, whether the inflammation be due to injury

or to disease, is the presence of what are known as colloid bodies; these are apparently droplets of myelin set free from the inflamed or degenerating white substance of Schwann, or, in some cases, it may be even from the degenerating axis cylinders; they stain deeply with picro-carmin, and may be readily distinguished in many pathological conditions.

The amyloid bodies which, in appearance and reactions differ somewhat from these colloid bodies, derive their name from the fact that they take on a deep brown stain when treated with iodine, and a bluish-violet with iodine and sulphuric acid; they are also deeply stained by logwood. They are somewhat like starch granules also, in that concentric circles are seen in them where the staining is not too deep, the centre always being much darker than the periphery. These amyloid bodies are of different sizes; they appear to be formed from red and white blood corpuscles, or even from connective tissue corpuscles which first become swollen and then granular; sometimes they remain homogeneous.

In the walls of the ventricles, in the connective tissue of the lining membrane of the ependyma, small granulations or masses of round cells are formed; these grow up beneath the epithelium of the ependyma, and project or break through the epithelial layer, until they form papilliform masses in which may be seen spindle-shaped cells, fibrillæ, and small vessels similar to those in the floor of a granulating wound. Pigmentation of the nerve cells is of frequent occurrence, not only in the ganglion cells at the base, but also in those of the cortical layers. The pigment is usually collected round the contractile nuclei; the cells may be undergoing fatty degeneration and even calcification, they may be vacuolated, or their processes may be much shorter than usual, and their protoplasm atrophied and granular—all the signs of atrophic change resulting from overwork, from prolonged stimulation, and from impaired nutrition. Earlier changes in the cells, such as cloudy swelling, have been observed, but these are seldom met with in specimens brought under the notice of the general pathologist. 'Wherever inflammatory changes are present in the brain, the Deiters' cells or neuroglia cells are always more abundant than usual. Between the connective tissue cell, consisting of a nucleus with little protoplasmic substance around it, which must be looked upon as a scavenging cell, and that with a large number of finely branched processes, cells in all stages of development may be seen.

ANATOMY OF THE SPINAL CORD

396. In order to render more intelligible the descriptions given of the pathological conditions found in the spinal cord, it may be well to describe very briefly the primary tracts of the cord, as the arrangement of these has to be constantly referred to in our study of the diseases of such a complicated structure. As many of the physiological data now at our command have been obtained by a study of pathological conditions met with in secondary degenerations (§§ 403 and 404), it may be stated generally that such secondary degeneration of the white matter of the cord extends in the same direction as the impulse which travels along the special tract in the normal cord runs; from this it may be deduced that the trophic centres are usually near the point at which the stimulating impressions are received or reflected. This may be best explained with the aid of a diagrammatic section of the cord.

In certain spreading lesions or secondary degenerations—locomotor ataxia, for instance—in which the primary lesion appears to be connected with the sensory nerves or the posterior nerve roots, there is an ascending degeneration along those definite tracts, marked in the diagram with an arrow pointing upwards. In lesions of the motor area of the brain, such as laceration produced by hæmorrhage, softening, or tumours, all of which are invariably followed by descending degeneration, we have the changes travelling along the tracts of white matter in the direction of the motor impulse—downwards—along those tracts marked with an arrow pointing downwards. If there be injury to the cord at any definite level,—an injury which may be traumatic or due to hæmorrhage or the growth of a tumour,—a secondary degeneration may be found passing from it upwards in the columns marked with an ascending arrow, and downwards in those marked with the descending arrow.

Descending tracts.—The most important of these is the *crossed pyramidal tract*, which, coming from the brain, crosses in the medulla oblongata at the decussation of the pyramids, and runs along the whole length of the cord in the position marked *c.r.p.* The *direct pyramidal tract* (*d.p.*) comes down from the brain through the medulla, but does not cross over to the opposite side: it forms a small strip which bounds the anterior median fissure and is found in the upper half of the cord only. Between these two pyramidal tracts, forming a connecting link, is a crescentic strip midway between the surface and

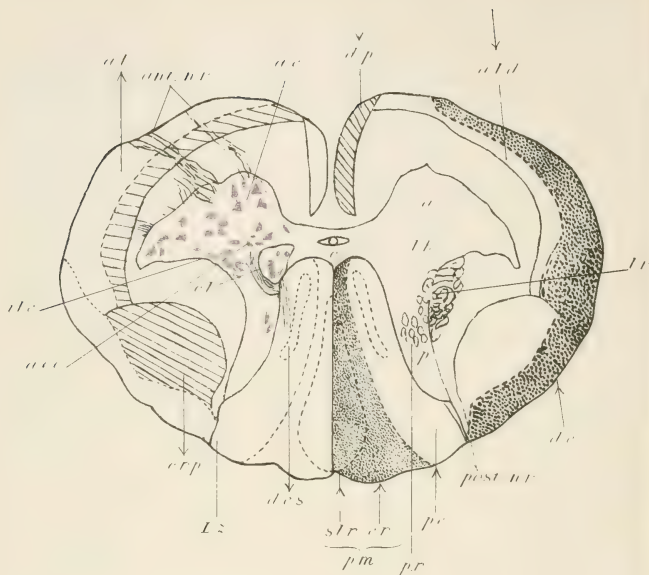


FIG. 203.—Diagram to illustrate the general arrangement of the several tracts of white matter, and of the multipolar cells in the grey matter in the spinal cord. Made up from a series of diagrams prepared by Dr. Sherrington, and given in Foster's "Physiology."

- c.r.p.* Crossed pyramidal tract.
- d.p.* Direct pyramidal tract.
- a.l.d.* Antero-lateral descending tract.
- d.c.s.* Descending "comma"-shaped tract.
- d.c.* Direct cerebellar tract.
- p.m.* Postero-median column, made up of sacral, lumbar, and dorsal root fibres, *s.l.r.*; and cervical root fibres, *c.r.*
- a.l.* Ascending lateral, or Gowers' tract.
- p.e.* Postero-external column.
- L.z.* Lissauer's zone.
- a.* Anterior horn of grey matter.
- a.c.* Multipolar ganglion cells of anterior horn.
- ant. n.r.* Anterior nerve root.
- p.* Posterior horn of grey matter, in which are a few nerve cells.
- post. n.r.* Posterior nerve root.
- l.h.* Lateral horn of grey matter.
- a.c.c.* Cells of the anterior cervix.
- c.l.* Clarke's column (or vesicular column).
- i.l.c.* Cells of the intermedio-lateral tract, or lateral horn.
- c.* Commissure or isthmus, in which is seen the central canal.
- l.r.* Lateral reticular formation.
- p.r.* Posterior reticular formation.

the anterior horn of grey matter. This is not a well-marked band, but it is spoken of as the *antero-lateral descending tract* (*a.l.d.*), as in it a number of altered fibres may be found in cords in which there is descending degeneration.

The only other area in which descending degeneration may be traced is the *descending "comma"-shaped tract* (*d.c.s.*), which is situated in the middle of the postero-external column. It probably represents part of the posterior root which first of all descends in the cord; degenerations in this area are, as a rule, extremely localised, running down only as far as the root fibres descend in each series of segments.

Ascending tracts.—The *direct cerebellar tract* (*d.c.*) is a mass of coarse white fibres, lying outside the lateral or crossed pyramidal tract immediately under the pia mater; it begins in the upper lumbar region, gradually increases in size as it passes upwards to the medulla, and ends in the restiform body or in the fibres that pass from that body to the cerebellum. Running along the whole length of the cord is a tract of very fine fibres arranged along each side of the posterior median fissure; it is spoken of as the *postero-median tract* (*p.m.*), or as the *postero-internal column* or column of Goll; it also ends in the medulla.

The *ascending antero-lateral tract*, or Gowers' tract (*a.l.*), is a comma-shaped area, the head of which lies between the direct cerebellar tract and the crossed pyramidal tract; this extends to the surface, and as far forward as the antero-lateral descending tract, outside of which it lies. It is made up of fibres of very different sizes. Outside the postero-internal column is the *postero-external tract* (*p.e.*), or Burdach's column.

The *posterior zone* (*L.z.*) or Lissauer's zone is a small tract just outside and behind the posterior horn of grey matter; it really belongs to the posterior root.

The parts of white matter immediately bounding the grey matter are not yet fully understood. The fibres do not degenerate either upwards or downwards, and, as suggested by Foster, they may be connecting fibres, each of which may be in communication with two trophic centres.

Speaking roughly, the *grey matter* of the cord is divided into anterior (*a.*) and posterior (*p.*) horns, and a commissural part (*c.*). It is made up of delicate nucleated neuroglia, in which bundles of medullated nerve fibres run in various directions, all apparently passing

from large multipolar nerve cells either across the commissural part or out into the nerve roots. There are also single nerve fibres, varying very much in size.

In the *anterior horn* (*a.h.*), embedded in the reticulum, are cells of considerable size (*a.c.*), which send out numerous processes into



FIG. 204.—Section of cord to show the structure of the anterior horn of grey matter. Stained by Weigert's method. ($\times 300$.)

- a.* Large multipolar nerve cell with branching processes.
- b.* Nerve fibres of white matter with myelin sheath stained.
- c.* Fibres running through the neuroglia in which the multipolar cells are embedded.
- d.* Process in which fibres of the anterior nerve roots run.

the surrounding grey matter; these cells are divided into smaller groups, named according to their position in the horn.

Clarke's column, or the vesicular column (*c.*), made up of cells, not quite so large as the above, embedded in a mass of fine fibrils, is situated outside the postero-external column, near the end of the

commissural part of the grey matter. In it the fibres of the direct cerebellar tract are supposed to take their origin.

On the outer side of the grey matter, about the level of the commissural part, is the *lateral horn (l.h.)*, the cells of which are somewhat spindle-shaped, "with their long axis placed transversely" (Foster). It is found as a special group only in the thoracic and lumbar regions.

Behind Clarke's column the cells of the *posterior horn* are few in number and comparatively small; they are branched and are found in all parts of the cord.

The cells of the *anterior cervix (a.c.)* are found, in the thoracic region only, as a group of small cells at the base of the anterior horn, just where it runs into the *commissure* or *isthmus (c.)*.

PATHOLOGICAL CHANGES IN THE SPINAL CORD

397. The pathological changes in the spinal cord may, for our purposes, be divided into five groups:—(1) Inflammation of the meninges; (2) inflammation of the grey matter or poliomyelitis (in which changes are set up in the ganglion cells, especially in those of the anterior horn); (3) atrophy, primary or secondary, of the tissues in the grey matter; (4) primary inflammation of the white matter of the cord; and (5) secondary degeneration of the white matter.

1. INFLAMMATION OF THE MENINGES

398. Here the processes correspond very closely to those met with in inflammation of the cerebral membranes; they may be confined to the membranes themselves; this, however, is rarely the case, owing to the intimate connection of the membranes with the surface of the cord; secondary inflammation in the periphery of the white matter of the cord, and also of the connective tissue of the nerve roots, usually supervenes, and these, in turn, may set up secondary degeneration.

2. INFLAMMATION OF THE GREY MATTER

399. The only cases of this condition that I have seen have occurred in children; it is certainly a disease of early life, though cases are recorded in which it has occurred in the young adult. It appears to be due either to actual hæmorrhage, or to a suddenly

increased blood pressure in a localised area, accompanied by great cedema of the surrounding tissue, and may be associated with the presence of micro-organisms.

The permanent symptoms are the result of destruction followed by absorption of a localised patch of grey matter; the fugitive symptoms are due, apparently, to pressure in the area around that in which the tissues are actually destroyed. On examining a cord in which there is inflammation of one or both of the anterior horns of grey matter, especially, as is often the case, where the patient has survived the onset of the disease for some time, there is usually a marked atrophy in some segment of the cord corresponding to the area and side of the muscles affected clinically; the affected side of the cord is considerably smaller, a diminution in size which appears to be due entirely to the atrophy of the anterior horn. This small horn is pinkish-grey and more gelatinous-looking than usual; it may be slightly pigmented.

Harden (§ 62 or 66) and stain (§ 130 or 142).

($\times 20$).—The horn on the affected side is atrophied and shrunken; the large ganglion cells can scarcely be made out; the network of the nerve fibres has almost disappeared, and its place has been taken by a connective tissue made up of proliferating neuroglia cells which take on the picro-carminic stain very readily. The anterior nerve roots are somewhat smaller than normal, and there is usually evidence of great congestion, the vessels being patent and filled with blood. In some cases small spaces filled with serous fluid may be seen.

($\times 300$).—Confirm the above appearances. The atrophy of the cells is well seen; these cells are irregular in shape, their processes are far less distinct than usual, there is an accumulation of pigment around the nuclei, and the spaces in which they lie may be considerably enlarged. Around the vessels there is an accumulation of young cells, though in some cases masses of small granules may be seen. In the later stages where atrophy is very far advanced, the whole of the nerve tissues, both cells and fibres, may be broken down, when, as in the brain, one of two things, or both, may happen, namely—the cyst (or series of minute cysts) containing serous fluid remains, or there is an enormous increase of the neuroglia which, becoming fibrillated and dense, and followed by contraction, is much more like ordinary cicatricial tissue than neuroglia.

3. SIMPLE ATROPHY OF THE GREY MATTER

400. This is usually well marked in the anterior horns. Little can be made out on naked-eye examination beyond the fact that the two sides of the cord are unequal, and that this inequality appears to be due to a diminution in the size of the anterior horn. This atrophy of the grey matter is found both in the cord and in the medulla oblongata, giving rise to various well-known forms of motor paralysis.

Harden (§ 62 or 66) and stain (§§ 102 or 104, 110 (*b*), and 132, and 140 or 142).

($\times 50$).—The anterior horn is atrophied, the ganglion cells are small, and have lost their plump outlines and processes. The nerve fibres are diminished in number, and many of those that remain take on stains very imperfectly. The anterior roots of the spinal nerves are smaller than usual, and in some cases nothing may be seen but a mass of pinkish (when stained, § 102 or 104) neuroglia.

($\times 300$).—Confirm the above appearances. The imperfectly stained cells, with their atrophied protoplasm and short blunted processes, are well seen; the nuclei, however, stain badly, and around each there is often deep pigmentation of the protoplasm; sometimes these large ganglion cells are represented merely by small granular masses of pigment. There is also a considerable quantity of pigment around the perivascular spaces, from which it may be gathered that at some earlier period inflammation or congestion must have played a prominent part in the process. There is also an increase of connective tissue around the nerves of the anterior spinal root, and in some cases we have a secondary degeneration of the descending or ascending columns of white matter, according to the position of the primary atrophy. When this atrophic process occurs in the medulla, descending degeneration of the pyramidal tracts is almost invariably met with.

4. INFLAMMATION OF THE WHITE MATTER

401. It is a somewhat difficult matter to determine how far inflammatory processes play any special part in the degenerations that take place in the nerves and in the columns of white matter in the cord. It has been found that in acute inflammation produced experimentally, there are changes both in the axis cylinder and in the myelin sheath which are said to be characteristic, but owing to the progressive nature

of most of these inflammatory diseases, it is extremely difficult to follow the exact course of events. It may be taken for granted, however, that in inflammation of the white matter there is distension of the vessels, exudation of leucocytes, impaired nutrition, degeneration of the myelin sheath, which may be gradually broken down, and irregular swelling and nodosity of the axis cylinder, followed by interruption at some point of its course, and ultimately by its disappearance, all this being accompanied or followed by a great increase of the neuroglia. Although some of these conditions are said to be primary, they may be best made out in secondary degeneration, such as is found in locomotor ataxia, the only difference being that in primary sclerosis the degeneration of the nerves and the increase of neuroglia go on simultaneously, whilst in secondary degeneration the increase of neuroglia appears to succeed the changes in the nerve fibres.

MULTIPLE SCLEROSIS

402. This may be looked upon as one of the forms of primary degeneration of the cord; it may also occur in the brain.

Naked-eye appearances.—On examining a cord in which there is multiple sclerosis, we find small grey gelatinous or opaque yellowish white patches, which stand out very prominently from the white matter of the columns.

On making sections at different levels, it will be found that these patches do not correspond in their localisation in the different parts of the cord; at one point they may be in the pyramidal tracts near the surface, at another, deep down, affecting one side or the other, whilst at a third level, some little distance away, the columns at the opposite side, or the posterior columns, may be affected. The grey matter may also be attacked, but this is somewhat more difficult to make out with the naked eye. The patches are usually rounded, though they may be somewhat irregular; they are gelatinous and marked with opaque areas, or they may be firm, sometimes almost like cicatricial tissue.

Harden (§ 62 or 66) sections from different levels, and stain (§§ 106 and 140 or 142).

($\times 15$).—Note the irregular distribution of the patches in the different specimens. It is evident that the disease is not confined to any special tract or series of tracts, either descending or ascending.

In carmine-stained specimens the degenerated areas stand out very prominently, the new connective tissue being deeply stained.

($\times 50$).—In the centre of one of these patches it is impossible to distinguish any nerve fibres lying in the dense felt-work of new connective tissue. Near the margin of the patch, however, a few



FIG. 205.—Section in the cervical region of the spinal cord from a case of multiple sclerosis. Stained by Weigert's method. ($\times 15$.)

In this section there is sclerosis more or less marked in every part of the cord, except in the direct pyramidal tracts (*a.*) on each side of the anterior median fissure.

b. Posterior nerve root.

c. Posterior median fissure.

d. Anterior horn of grey matter.

comparatively normal nerve fibres, or fibres in which the myelin is undergoing granular degeneration, may be seen. In the vessels the lumen is somewhat more patent than usual, and there may be hyaline thickening of the inner coat, or thickening of the adventitia.

($\times 300$).—Confirm the above appearances. Note first the dense felted network of neuroglia in which the nuclei of the cells may be

distinguished surrounded by a small quantity of protoplasm from which run out numerous branching processes (see Fig. 202). Embedded in this network are a number of compound granular corpuscles which give a black reaction with osmic acid. The axis cylinders of the nerve fibres may be seen in the margin of the patch, and between them the increased amount of neuroglia can be readily made out. Note the hyaline thickening of the intima with a similar change in the connective tissue of the muscular coat; there is also an increased quantity of

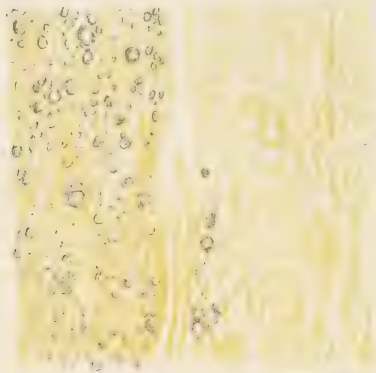


FIG. 206.—Portion of the postero-internal column of a sclerosed cord from a case of locomotor ataxia. Stained by Weigert's method. ($\times 300$.)

- a.* Comparatively healthy fibres, of which the myelin sheaths are stained.
- b.* Reticulum of neuroglia unstained by the hæmatoxylin.

connective tissue in the adventitia. The perivascular lymph spaces may be considerably enlarged and filled with small round cells, or with cells containing fatty particles which are well brought out by osmic acid. Corpora amylacea (§ 395) may also be made out, whilst where the process is not far advanced, and where the remains of degenerating nerve fibres can still be seen, the compound granular corpuscles and fatty granulations are present in very considerable numbers, not only in the spaces between the neuroglia, but also in the perivascular lymphatics.

5. DESCENDING DEGENERATION

403. Descending degeneration follows destruction or injury of the hemispherical ganglia in the region of the fissure of Rolando (the motor area); of the fibres that run from these ganglia as they pass through the corona radiata; of the internal capsule; or of the motor tract below this point. If such injury be on the left side, say, the degeneration is found first in the motor area (pyramid) of the same side, in the medulla oblongata. Below the point of decussation of the pyramids the lesion is seen in the following positions—first, in the direct pyramidal tract on the same (left) side; second, in the crossed pyramidal tract on the opposite (right) side, situated in the postero-lateral part of the antero-lateral column, where it does not come quite to the surface, but is bounded externally by the direct cerebellar tract; and third, in the antero-lateral descending tract. When this degeneration depends upon injury of the cord, the direct pyramidal tracts are affected for a short distance only, whilst the comma-shaped tract in the posterior column—the posterior root fibres, which, as already seen, run down the cord for some distance—is also involved.

Naked-eye appearances.—The principal change is a peculiar firmness to the touch of the affected areas, which assume a much greyer and more gelatinous appearance than the corresponding areas on the opposite side.

Harden (§§ 11, 62–66), mount one section unstained (§§ 41, 86, and 87), stain others (§§ 104, 106, 110 (*b*) and 132, 139, 140, and 376), and mount (§§ 193 and 199).

Hold the unstained section up to the light, and note that in the crossed pyramidal tract the tissue is much more transparent than the other white matter; it looks almost like grey matter. This change is not so readily recognised in the direct pyramidal tract, which is very small; in some cases it is represented by a few fibres only.

($\times 50$).—In the stained specimen (§ 106) note that in the affected areas (the left direct and right crossed pyramidal tracts) the tissue is much pinker than is the normal white nerve tissue. There appears to be a marked increase in the amount of neuroglia, with a corresponding diminution in the number and size of the nerve fibres.

($\times 300$).—The increase in the amount of neuroglia can be very readily made out, especially in the carmine and osmic acid stained specimen. The myelin sheath of the nerve is breaking down or has

disappeared, but the axis cylinder, deeply stained, can often be easily distinguished. In sections it will be noticed that the affected area is not nearly so deeply stained by osmic acid as is the part where the fatty myelin sheath is still present.

Examine a fresh section of a similar cord—or one in which the degeneration is not so far advanced, which is softer, and not so transparent, or a section prepared by Marchi's method (§ 67).

($\times 6$).—The fatty degeneration is well seen in the crossed pyramidal tract.



FIG. 207.—Transverse section of the spinal cord from a case of hemiplegia, descending degeneration well marked in the crossed pyramidal tract. Stained by Marchi's method. ($\times 6$.)

Note that the altered myelin now takes on the black reaction of fatty degeneration.

($\times 300$).—In the affected area are numerous bodies about three times the size of a red blood corpuscle. Each of these contains two or three nuclei. Also observe the compound granular corpuscles; myelin drops, rounded or tadpole-shaped; colloid masses, few in number—probably derived from the axis cylinder or myelin sheath, and unstained by iodine—and a few small beaded fibres. In the perivascular sheaths fatty globules and granules can frequently be seen, especially in the specimens stained with carmine and osmic acid; but few of the above

bodies can be made out in a hardened specimen of the cord except when hardened by Marchi's method.

This descending degeneration, then, is simply a secondary degenerative process extending along the nerve fibres, accompanied by a formation of neuroglia, which appears as a "replacement" product.

LOCOMOTOR ATAXIA AND ASCENDING DEGENERATION

404. In disease of the peripheral sensory nerves or of the posterior root fibres of the spinal nerves, from which these are given off, or when there is injury of the posterior columns of the cord, secondary degeneration appears in certain areas above the seat of lesion. In locomotor ataxia the process is essentially a progressive one; but in secondary degeneration, due to injury of the cord, the degeneration is very rapidly developed in all the parts that are ultimately affected.

In this latter case both the postero-internal and postero-external tracts degenerate for some distance, but higher up the postero-internal tract, which appears to be the main path of upward conduction, alone is affected, as far up, however, as the funiculus gracilis.

Naked-eye appearances.—In a section of an ataxic cord, made at about the level of the last cervical or first dorsal nerve, it will be seen that the dura mater and pia mater are thickened—the posterior nerve roots are small and transparent, and the posterior columns are grey and gelatinous in appearance, but firm in texture. The thickened pia mater is firmly adherent to the posterior columns.

Prepare as above (§ 402 or 403).

($\times 15$).—In the postero-external columns, immediately internal to the posterior roots, there is an increase of fibrous tissue or neuroglia, which takes on the carmine stain deeply; stained by Weigert's method the tissue appears much yellower than normal, and with osmic acid the blackening is not nearly so marked as in the normal white tracts. When the change is confined to this region the disease may be spoken of as locomotor ataxia pure and simple. It will be found, however, that in most cases there is a secondary degenerative process which extends along the sensory tracts, and therefore passes upwards. This results in an increased connective tissue formation, with corresponding changes in the nerve fibres. These changes must be looked for in the inner parts of the postero-external columns, in the postero-internal columns, and, in the upper part of the cord, in the direct cerebellar

tracts; whilst Gowers and Haddon describe also an affected comma-shaped area opposite the outer angle of the anterior horn of grey matter, either at the surface in the dorsal region, or close to the surface at the level of the cervical enlargement. In all these areas there is a



FIG. 208.—Section taken from the dorsal region of an ataxic cord.
Stained by Weigert's method. ($\times 15$.)

- a.* Anterior median fissure.
- b.* Anterior horn of grey matter.
- c.* Anterior nerve root.
- d.* Posterior nerve root, running from the posterior horn of grey matter.
- e.* Column of Burdach, or postero-external tract undergoing secondary degeneration.
- f.* Column of Goll, or postero-internal tract in a still more advanced stage of degeneration.
- g.* Posterior median fissure.

The direct cerebellar and Gowers' tracts are unaffected.

new formation of fibrous tissue which takes on a deep pink when stained with picro-carmin.

($\times 50$).—Scattered at irregular intervals through this pink tissue are more opaque patches—collections of breaking-down axis cylinders or colloid bodies derived from altered nerve fibres. Near the surface the vessels are considerably congested, their walls are thickened, and the perivascular spaces are filled with granular masses. Where the

disease is furthest advanced, *i.e.* in some parts of the postero-external columns, the axis cylinders have disappeared.

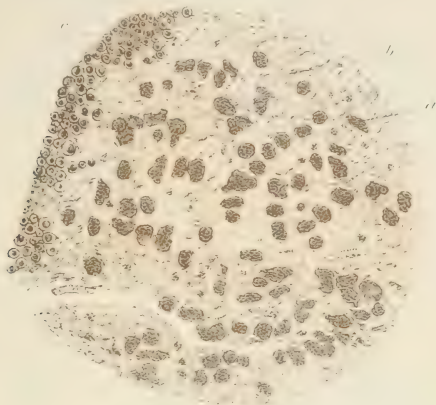


FIG. 209.—Locomotor ataxia. Small portion of nerve tissue from the direct cerebellar tract. Stained with carmine. ($\times 120$.)

- a.* Compound granular corpuscles and colloid bodies.
- b.* Newly formed fibro-cellular tissue (pink).
- c.* Healthy nerve fibres.

($\times 300$).—Note the distended vessels. In the perivascular sheath there is a considerable quantity of fat in the form of granules and globules, stained black with osmic acid. Around the distended blood vessels, leucocytes may be seen. This loading of the connective tissue with cells is also seen in the pia mater, where the perivascular spaces are filled with fatty particles, and in some instances there is, in the vessel itself, a substance giving, with osmic acid, a black reaction.

In longitudinal and transverse sections, examine the nerves of the affected areas. In these are very marked changes, such as are found in most cases of myelitis or inflammation of the cord. First a number of constrictions may be seen at intervals (in the longitudinal section) along the axis cylinder, the myelin being, apparently, but slightly affected, in other cases remaining intact. Later, the alternate constriction and swelling are more pronounced, and the varicosity is very marked. At other points the swollen masses of axis cylinders are seen to be vacuolated, and in other parts they form the granular masses seen

scattered throughout the fibrous tissue. Where these are seen in a transverse section of the cord, or where the disease is not very far

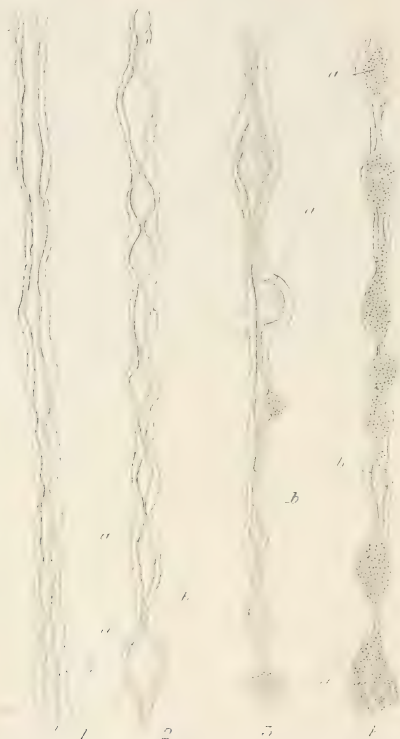


FIG. 210.—Locomotor ataxia. Nerves in various stages of degeneration, from the postero-external columns in the cervical region of the cord. Stained with osmic acid. ($\times 400$.)

- a.* The axis cylinders become more and more swollen and constricted, and then undergo fatty degeneration.
- b.* Nerve sheath, which gradually loses its distinct outline and becomes fatty and granular.

advanced, the colloid bodies are very readily recognised by their clear homogeneous appearance, and often by their large size.

In the above condition be careful to distinguish between the area

of the primary disease—the outer part of the postero-external columns—and those affected by a secondary ascending degeneration—postero-internal, direct cerebellar, and Gowers' and Haddon's tracts—all of which may be affected *above the point of primary lesion* as the result of any injury to the cord.

In examining this section, a careful search should be made for

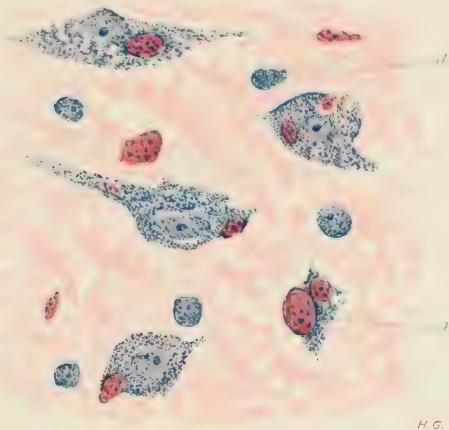


FIG. 211.—Smear preparation of the cornu ammonis of a dog suffering from rabies. Stained by Williams and Lowden's method. ($\times 800$.)

- a. Nerve cell with vacuolated space or "court" round the nucleus. A small Negri body is seen at one extremity of the cell and another in the axial process of the cell.
- b. Two large Negri bodies almost filling a vacuolated nerve cell.
- c. A free Negri body with its basophile bodies.
- d. Nucleus of a "glia" cell.

similar changes in Clarke's column, and for altered conditions in both the posterior and anterior horns of grey matter, and for pigmentation, or swelling of the nerve cells.

Varicose swelling of the axis cylinder and hyaline thickening of the sheath, with increase in the amount of neuroglia and colloid bodies, may also be found in the following positions in well-marked cases of locomotor ataxia: optic tracts and nerves, auditory nerve, and stria

acousticæ, fifth nerve, fourth nerves, at their decussation in the valve of Vieussens, corpora quadrigemina in the roof of the aqueduct of Sylvius, and the roots of the hypoglossal nerves.

THE NERVE CENTRES IN RABIES OR HYDROPHOBIA

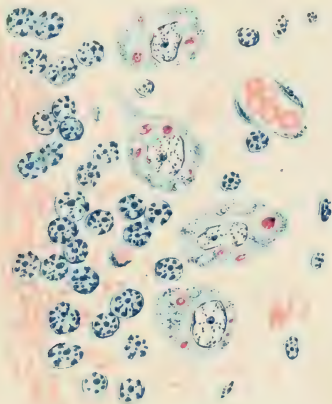
405. Negri's observations have given an additional interest to the morbid histology of the brain and cord in hydrophobia. To the naked eye there is usually marked congestion and œdema both of the brain and spinal cord and of the meninges. In some cases meningitis is a very marked feature, fibrinous lymph being found in the pia arachnoid spaces and on the arachnoid surface. Small hæmorrhages into the cerebral ventricles, and on the surface, and in the substance of the medulla oblongata and spinal cord are often found.

($\times 50$).—In addition to the small hæmorrhages above described, collections of leucocytes are met with in hyperæmic areas in the medulla oblongata and pons, sometimes in the cerebral tissue and in the spinal cord, in the perivascular lymphatics of the grey matter of the anterior horns, and in the white matter of the postero-internal and postero-external columns. Here also the nerve cells are seen to be vacuolated, hyaline and granular, and often pigmented; thrombi may be present in some of the smaller vessels, and the collection of leucocytes may be so prominent, especially in the medulla, that they have been spoken of as "miliary abscesses."

($\times 800$).—Go over the above features, and in addition make a careful search for "Negri" bodies, which certainly appear to be characteristic of this disease. Stain (§ 146) and mount (§§ 193 and 199).

Lying in the cytoplasm of the nerve cells or in their branches, or in some cases outside them, are rounded, oval, triangular, or slightly spindle- or sausage-shaped bodies—Negri bodies—which taking on an eosin ground stain are studded with basophile granules, rods, and "circles." These bodies are from 0.5μ to 20μ in diameter, the size increasing with the period that the disease has run, the larger forms seldom being met with in specially susceptible animals. In some cases these bodies may be constricted in the middle, or, if somewhat elongated, there may be two or three constrictions. They may be met with in almost all the nerve cells of the central nervous system

in cases of hydrophobia, but are most numerous, and found most readily, in the cells of the cornu ammonis; they may also be found in the Purkinje cells of the cerebellum. The basophile granules, rods, or "rings" are often situated within vacuoles; a small central body, which is surrounded by no clear space, is stated to correspond to a protozoan nucleus; this, however, can be little more than a suggestion. These Negri bodies certainly appear to be specific to hydrophobia;



H. G.

FIG. 212.—Section of the cerebellum from a case of rabies in the dog.
Stained by Williams and Lowden's method. ($\times 800$.)

- a.a.* Purkinje cells, in which are seen small Negri bodies.
- b.* Larger Negri body with central body surrounded by red clear space.
- c.* Small blood vessel containing red blood corpuscles—endothelial lining well seen.
- d.* Nucleus of "glia" cell.
- e.* Nuclei of the "nuclear layer."
- f.* Capillary vessel.

they are present in large numbers even at a very early stage of the disease, but are then so small that they may easily escape detection: they may be so small indeed that they may pass through the pores of a Berkefeld filter. Later, and this of course is best seen in the more chronic cases, they attain a considerable size, and have the appearances presented in Figs. 211 and 212.

WAXY DISEASE OF THE CORD

406. Waxy degeneration of certain elements of the cord is comparatively rare. Prepare (§§ 58-64), cut (§ 82 *et seq.*), stain (§ 117), and mount (§ 195). Notice first the affection of the middle coat of the vessels, then the degeneration of the connective tissue fibres, of the processes and even of the bodies of the ganglion cells, all of which are swollen and stained red violet.

TUMOURS GROWING IN CONNECTION WITH THE MEMBRANE OF THE BRAIN AND CORD

407. *Syphilitic gummata* occur in the dura mater, in the pia mater, and in the cerebral substance, near the base of the brain, especially in the interpeduncular space. *Glioma* and *myxoma* in various forms, *sarcoma*—melanotic, spindle-celled, and small round-celled (the latter usually seen as a primary growth in children), *myxosarcoma*, *angioma*, *psammoma*, *fibroma*, and more rarely *osteoma* and *lipoma*—all occur in the central nervous system. *Carcinoma* is almost invariably secondary. In addition to the above—which, with the exception of the glioma, occur in both brain and membranes,—*chondroma* is found growing in the meninges. Dermoid cysts are described as occurring in the brain and dura mater. (See Chapter XIV.)

Parasites—*Cysticercus cellulosæ* and hydatid cyst. (See Chapter XI.)

RETINA

408. Harden the retina for examination (§§ 59 and 62). If the whole eye can be obtained, place it intact in the hardening fluid, or make a few minute punctures in front of the attachment of the cornea. Treat as for nerve tissues (§§ 102, 110 (*b*) and 132, 140, and 142). If the posterior half of the eye only can be obtained, turn the tissues inside out, *i.e.* have the retina on the convex instead of the concave surface before placing in the hardening fluid. In this way it is kept tense, and much better preparations will be obtained. In place of Müller's fluid, a 10 per cent. solution of chloral hydrate may be used in the same way.

The peripheral nerves are to be treated generally in the same way as pieces of spinal cord.

CHAPTER XIII

THE ORGANS OF GENERATION IN THE FEMALE ¹

THE PELVIC PERITONEUM AND CONNECTIVE TISSUE

409. The peritoneum lining the true pelvis is frequently the seat of an inflammatory process—*pelvic peritonitis* or *perimetritis*. As a remote result, it is not uncommon to find, on post-mortem examination, considerable alterations from the normal relationship of the parts, due to the presence of bands of adhesion. Such adhesions play an important part in the production of certain pathological conditions, notably displacement of the uterus and obstruction of the Fallopian tubes. Thus the fimbriated extremity may adhere to the inflamed peritoneal surface, or obstruction of the tube may be occasioned at some other point in its course. The whole or a portion of the tube is thus transformed into a closed sac, in which secretions accumulate, and a cystic condition is developed. Adhesions between the uterus and neighbouring parts may lead to displacement and fixation of that organ.

Beneath the peritoneum there is a layer of loose cellular connective tissue. Between the layers of the broad ligaments, especially at their bases and where they are reflected on to the uterus, and around the cervix, and behind it, the cellular tissue is present in considerable quantity. This tissue is particularly rich in lymphatic vessels and glands, and is frequently the seat of inflammatory action, constituting the condition known as *parametritis* or *pelvic cellulitis*. By direct continuity the process may spread under the peritoneum to the abdominal wall, or up the line of the ureters towards the kidneys. Such deposits may suppurate, and occasion pelvic abscesses which

¹ Written originally by J. Milne Chapman, M.B., M.R.C.S., for the Second Edition. In the revision of this chapter I am indebted for much valuable assistance to T. Watts Eden, M.D., F.R.C.P.

may open through the abdominal wall, or into the bowel, bladder, or vagina. It should be noted that these conditions of pelvic peritonitis and cellulitis seldom occur entirely independent of one another, and it is sometimes impossible to tell, on post-mortem examination, which structure was primarily involved.

PELVIC HÆMATOCELE

410. Effusion of blood may occur into the pelvic peritoneal cavity (intra-peritoneal hæmatocele) or into the sub-peritoneal connective tissue (extra-peritoneal hæmatocele). The former is due, in the great majority of cases, to hæmorrhage from a gravid Fallopian tube (extra-uterine gestation), the actual cause of the bleeding being tubal rupture or tubal abortion. It may also occur from the slipping of ligatures after surgical operations upon the pelvic organs, from the rupture of varicose veins of the broad ligament, and possibly also from a ruptured Graafian follicle. The latter is of rarer occurrence than the former, and may be caused by extra-peritoneal rupture of a gravid tube, or by injury in labour to the lower uterine segment, cervix, or vagina; in the latter case, a vaginal or labial hæmatoma results.

Blood effused into the pelvic peritoneal cavity collects in the pouch of Douglas, forming a retro-uterine swelling. If the amount is insufficient to endanger life, it becomes rapidly shut off from the general peritoneal cavity by the formation of a roof of omentum and coils of intestine, which, by plastic peritonitis, adhere to one another, and to the anterior and lateral abdominal walls, thus limiting the effusion to the pelvis. Blood effusions thus limited usually coagulate, and become slowly absorbed in the course of several weeks, or it may be months. They may, however, remain fluid, and resist absorption altogether, or in very rare instances they may suppurate, giving rise to a pelvic abscess. Adhesions left after the absorption of blood effusions are inconsiderable.

Extra-peritoneal effusions are more rapidly absorbed, and show even less tendency to become infected.

MICROSCOPIC STRUCTURE OF THE WALL OF THE NORMAL UTERUS

411. ($\times 50$).—Examine a section made through the whole thickness of the uterine wall.

The peritoneal lining is seen as a thin layer covering the outer surface. Beneath this is a small quantity of condensed fibrous tissue, but the main bulk of the wall is composed of bundles of non-striated muscle running in various directions, with a supporting framework of connective tissues, partly structureless, partly fibrous. In the wall there are numerous large vessels and lymph spaces. For a depth of 1 to 2 mm. from the internal surface is the "mucous membrane," but no submucous structure is present, nor can the two layers, mucous and muscular, be sharply differentiated. The mucous membrane consists of connective tissue of an embryonic type, with large nucleated round or slightly spindle-shaped cells. No large vessels are visible, the mucous membrane being supplied entirely by capillaries.

($\times 450$).—Notice, here and there, a few ordinary connective tissue fibres and some non-striated muscle cells, especially in the deeper layer. The free surface is covered with a single layer of ciliated columnar epithelium, which is prolonged downwards as the lining of test-tube glands, the deep ends of which are lost sight of among the superficial layers of the muscle tissue. The direction of these glands is very varied, and a complete section of the whole length of one is seldom obtained. They are occasionally somewhat spiral, usually simple, but sometimes slightly branched. The epithelium lining the glands is similar to that covering the free surface, but is devoid of cilia.

NOTE ON THE APPEARANCE OF THE MUCOUS MEMBRANE OF THE UTERUS DURING MENSTRUATION

412. The question of menstruation has been recently studied by Gibbard and others in human uteri removed during a menstrual period. The earliest changes appear to be hyperemia and swelling of the mucosa associated with engorgement of blood vessels, which is most marked in the superficial capillaries. The glands become elongated and slightly dilated, presenting a corkscrew outline, and the interglandular connective tissue increases in amount, becomes looser in texture, and sometimes shows traces of leucocytic infiltration. A little later small interstitial hæmorrhages appear, situated chiefly beneath the superficial epithelium, and as a result patches of cells are thrown off, but the amount of tissue lost in this way is inconsiderable. It is



FIG. 213.—Section from surface to surface of the uterine wall of a girl aged sixteen, who had never menstruated. ($\times 20$.) Logwood and eosin.
a. "The mucous membrane." *b.* Epithelium covering the cavity surface.
c.c. Uterine glands. *f.* Muscular wall, with muscle bundles cut in various directions. *d.* Vessel. *e.* Lymphatic space. *g.* The peritoneal surface covered with flattened endothelioid cells.

uncertain whether the interstitial hæmorrhages are due to diapedesis or to degeneration and rupture of the walls of the capillaries.

METRITIS

413. Metritis is an affection of the connective tissue stroma which is present both in the muscular and in the mucous layers of the uterus. When the inflammation is acute, purulent infiltration of the uterine wall may occur. When the affection is chronic, there is first an increase in the quantity of embryonic elements throughout the whole muscular wall, especially in the neighbourhood of the blood vessels, followed by a development and contraction of connective tissue around the vessels and lymph spaces, leading to dilatation of the latter.

ENDOMETRITIS

414. Remove with a curette a portion of the endometrium from a case of endometritis. Harden (§ 61, 62, or 64) and stain (§§ 103 or 110 (b) and 132).

($\times 50$).—There is usually considerable dilatation of the glands, which, instead of being regularly shaped tubes, with the walls almost in apposition (Fig. 213), appear as convoluted spaces, with the epithelium in a more or less catarrhal condition. The matrix is looser in texture than normal, with here and there spaces and extravasations of blood, the latter sometimes tearing the structures asunder, at other times simply infiltrating them. The individual cells are swollen and granular, and have large and particularly well-stained nuclei. Numerous dilated capillaries, some distended with blood, may also be seen.

In more chronic cases of endometritis, the catarrhal condition of the glands often leads to loosening and probably shedding of their epithelium. The cells of the matrix become fibrillated, and new connective tissue develops, apparently at the seat of extravasation, and later the whole matrix becomes fibrous instead of cellular. As this new tissue shrinks, it either, if in large quantity, encroaches on the gland spaces, or, if in small quantity, separates their walls and leads to detachment of the epithelial lining cells.

Polypi of the cervix may be either mucous, adenomatous, or fibroid. Fibroids are rare; they are similar in structure to fibroids of the

body of the uterus. The mucous variety is common, and occurs as small papillary outgrowths, seldom larger than a pea, attached to one or both lips of the cervix; they are usually associated with chorion

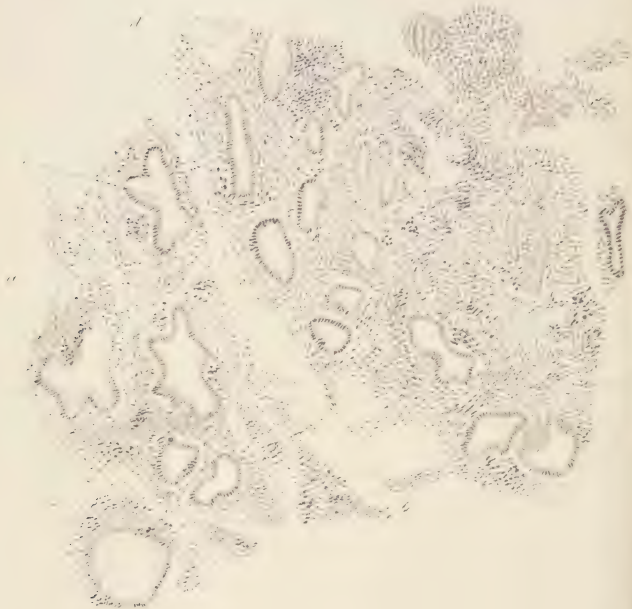


FIG. 214.—Section of curetted fragment from a case of endometritis resulting from abortion, which occurred four months prior to the curetting. Stained with logwood. ($\times 50$.)

- a.* Matrix with nuclei deeply stained.
- b.* Commencing fibrillation of cells of matrix.
- c.* Dilated glands.
- d.* Space from which a gland has fallen.

endometritis. Adenomatous polypi are also rare, and consist of hypertrophied mucous membrane, with enormously dilated and branching gland spaces lined with cylindrical epithelium.

CERVICAL CATARRH ; EROSIONS, ECTROPION, AND SO-CALLED
ULCERATION

415. To obtain satisfactory preparations of the above conditions it is absolutely essential that portions of the cervix be removed during life and carefully hardened (§§ 61-64), otherwise the epithelial lining of the canal and of the erosions will be lost, and a fallacious appearance produced. On examining stained sections (§§ 103 or 110 (*b*) and 132) of a piece of one of these "ulcers," the surface is found to resemble very closely the mucous membrane of the cervix; it is thrown into papillary folds, and is covered by a single layer of cubical epithelium. Deeper down are irregular spaces, lined with similar epithelium, which appear to have been formed from the deep extremities of the foldings between the papillæ. Should the section be made at the point of continuity between the erosion and the healthy vaginal aspect, it will be seen that the change from the one kind of epithelium to the other is very gradual; and, indeed, it is believed that such erosions result from a loss of the superficial squamous layer down to the deepest cells, a single layer only being left. It is more probable that the condition arises from a proliferation outwards of the cervical canal epithelium, which comes to occupy the place of the squamous epithelium on the vaginal aspect. Such erosions are usually associated with catarrh of the cervical cavity. The microscopic appearances of the cervical mucous membrane, under these circumstances, closely resemble those just described as characteristic of erosions. Another way in which cylindrical or cubical epithelium comes to cover the portion of cervix exposed to the vagina is by the healing of lacerations made during delivery. The cubical epithelium proliferates more rapidly than does the squamous. Should the lacerations be extensive and fail to heal by first intention, the lips of the cervix become separated from each other, the lower end of the cervical canal gets everted, and the torn surfaces derive their epithelial covering from that of the latter, and thus become covered with imperfect cylindrical, *i.e.*, cubical cells. In those new glandular structures (erosions) on the vaginal aspect, however originating, there is, in addition to the alteration on the surface, a proliferation of the subjacent connective tissues, and it is to outgrowths of this, rather than to foldings from the surface, that Fischel attributes the papillary formation. When the deep ends of the foldings become shut off, retention cysts are produced, which may

bulge out the portions still covered by squamous epithelium, reach



FIG. 215. — Cervical erosion. *a.* Point of junction of healthy cervix with eroded surface; to the left of *a*, squamous epithelium of the vaginal aspect; to the right of *a*, eroded surface covered by a single layer of cubical cells (slightly diagrammatic). *b.* Normal tissue of the cervix. *c.* New glandular formation, passing at *d* beneath the healthily covered surface. Stained with logwood. ($\times 50$.)

the surface, rupture, and thus occasion an extension of the altered condition.

NEOPLASMS—NEW GROWTHS OF THE UTERUS

416. Polypi of the cervix uteri have already been referred to. Fibroid tumours—myomas—will be described in the chapter on Tumours. It must here be noted that the myoma is frequently the seat of cystic degeneration; such a tumour is of rapid, often irregular growth, and it differs from the ordinary fibroid in the fact that its growth frequently progresses after the menopause, and after removal of the ovaries, while the simple myoma almost invariably ceases to grow, and often undergoes retrogressive changes and diminution in bulk under similar circumstances.

Polypi of the uterus may be either innocent or malignant. Innocent polypi may be either mucous or fibroid; the latter project into the cavity of the uterus, and have either been pedunculated originally, or have become so as the tumour has increased in size. Malignant polypi are associated with more extensive malignant disease of the uterus, to be presently described.

CANCER OF THE CERVIX UTERI

417. Two varieties of cancer occur in the cervix with almost equal frequency: *adenocarcinoma* arising in the glands, and *squamous-celled carcinoma* (epithelioma) arising at the margin of the external os uteri. They can only be distinguished by microscopic examination of the growing edge of the tumour. The growth arises most commonly in the portio-vaginalis cervicis, but may also occur in the supra-vaginal portion of the cervix. The disease may assume three different clinical types, (a) the *proliferative* type, in which large masses of new growth are formed which project into and fill up the vaginal vault; (b) the *destructive* type, in which the growth is more diffused and rapidly undergoes ulceration, leading to the formation of large ragged cavities; (c) sometimes the disease begins in the mucous membrane of the cervical cavity; but little deformity is then produced until it has made considerable progress, when thickening and induration of the cervix will become recognisable.

The pelvic cellular tissue and the pelvic and abdominal glands soon become affected, and, as the disease progresses, ulceration both of the vaginal aspect and of the cavity occurs, and the vagina and neighbouring organs become implicated. The base of the bladder is implicated

comparatively early, owing to its anatomical relation to the cervix and anterior vaginal wall; extension to the rectum only occurs in more advanced cases.

The microscopic structure of the diseased parts resembles that of the corresponding malignant growths and infiltrations in other positions. (Chapter XIV.)

CARCINOMA OF THE BODY OF THE UTERUS

418. This is comparatively rare, and is chiefly a disease of advanced life. It occurs either as a nodule formation under the mucous membrane, or as a polypoidal outgrowth, originating probably in the uterine glands, and bulging into the uterine cavity. The progress of these cases is much slower than that of the cervical cases already described.

CHORION EPITHELIOMA

419. Synonyms, "Deciduoma Malignum"; "Syncytioma Malignum"; "Carcinoma Syncytiale." Chorion epithelioma is a malignant tumour arising either in immediate, or more or less remote, connection with pregnancy, and situated usually, but not invariably, in the uterus; it has been found in the testicle. In the uterus it forms a hæmorrhagic growth occupying the usual site of the placenta, *i.e.* the fundus and adjacent portions of the anterior and posterior uterine walls. The primary growth may, however, be situated in the vaginal walls, the *labium majus*, the Fallopian tube, or the ovary. Metastatic growths are quickly formed, and in many cases this tumour destroys life with almost unexampled rapidity. After much discussion, and many contradictory observations, it has now been definitely accepted that it arises from the chorionic epithelium, both layers of which are represented in the specific cellular elements of the tumour. It is, therefore, clearly embryonic, not maternal in origin.

Chorion epithelioma is essentially a disease of fertile women, and pregnancy is its necessary antecedent. In 40 per cent. of the recorded cases a hydatidiform mole has been found in the immediately preceding pregnancy. It has been observed that cysts of the corpus luteum occur in association with both hydatidiform mole and chorion epithelioma with remarkable frequency.

This tumour usually occurs as a soft, spongy, friable mass, almost

like a large blood clot, lying in the cavity or sometimes in the muscular wall of the uterus, or in the above-mentioned positions.

In this are paler patches and strands, some of which are yellow and opaque, and appear to be the result of necrotic changes in the tumour. Others of the paler gelatinous masses appear to be the rapidly growing tumour tissues. Even in the paler patches the tissue is very vascular, and the degeneration appears to favour extensive hæmorrhage. Metastatic growths may appear in the lung at a very early stage, the tumour cells being conveyed from the original tumour by the blood stream. In connection with this it should be noticed that the growing tumour seems to have a special power of invading all the tissues, but especially the blood vessels. In some cases, however, the growth may remain strictly localised.

Harden (§ 59, 62, 63, or 64), stain (§§ 102, 110 (*b*) and 132, 146, 164), and mount (§ 195 or 199).

($\times 50$).—Embedded in a mass of blood clot and granular débris, the remains of degenerated tumour, is a tissue which at once suggests the origin of the growth from the chorionic villi. Nucleated protoplasmic masses resembling the syncytial cells can usually be seen in the tumour, whilst accompanying these are groups of small cubical or polyhedral cells with comparatively large nuclei, seen lying in groups with no connective tissue between them. Here and there a few large mononucleated cells may be seen. In some cases structures resembling chorionic villi with syncytial and Langhans' cells with almost normal arrangement may be seen. Hæmorrhages and collections of fibrin and leucocytes are seen scattered throughout this tissue.

($\times 300$).—The different types of cells may now be readily made out. The plasmodial or giant cells, with their many nuclei and clear hyaline protoplasm, are usually seen at the margin of the tumour mass, whilst beneath these, and closely packed in groups of considerable size, are globose or polyhedral cells with clear cytoplasm and rounded or oval faintly staining nuclei in which there is a distinct chromatin network. These are said to be derived from the Langhans' cells of the chorionic villi. Large wandering cells, derived from the investing cells of the chorionic villi, which are said to have great powers of invading and destroying the tissues, may also be seen in this tumour. Note the marked vascularity of the growth, the extensive granular degeneration of the tissues, especially where these seem to be growing most rapidly, and the numerous hæmorrhages and masses of fibrin

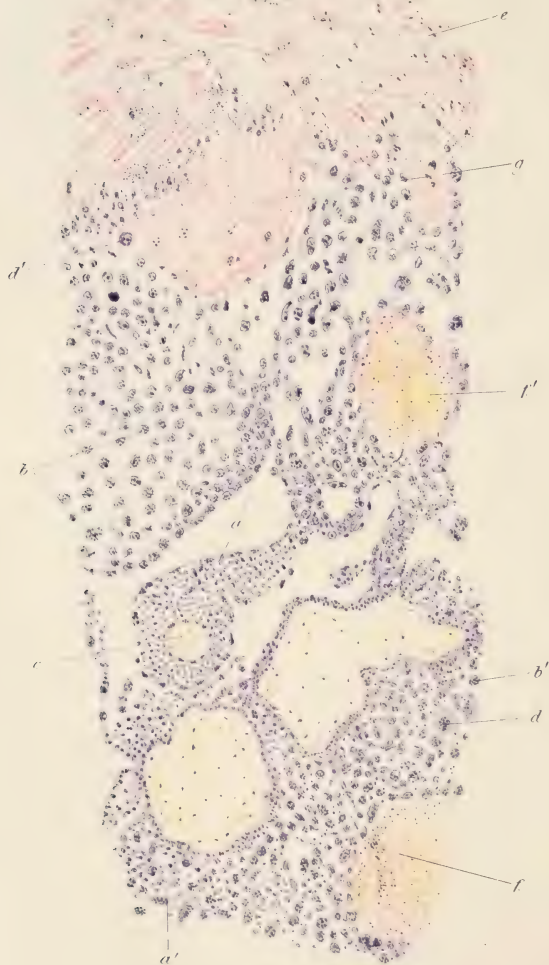


FIG. 216.

that are to be seen either in dilated sinuses or in the degenerating tumour tissue. Various modifications of the above structure may be met with, but the types of cells present always remain the same.

SARCOMA

420. Tumours of a sarcomatous character in the walls of the uterus often resemble fibroids, except in so far that they are devoid of any capsule. Portions of a fibroid tumour may undergo sarcomatous degeneration. The sarcomatous spindle cells then differ from the myomatous in their greater size, and in the greater size and more oval shape of their nuclei. Sarcoma also occurs as a primary disease in the mucous membrane, usually in that of the body, rarely in that of the cervix. The mucous membrane is irregularly polypoid, pulpy, and brain-like; the uterus is enlarged, and its cavity elongated. The embryonic connective tissue, forming the stroma of the mucous membrane, is greatly increased in quantity, and is closely packed with round and occasional spindle-shaped, large nucleated cells, while the epithelial surface of the uterine cavity is extensively destroyed, when the diseased structures become exposed or ulcerated.

DISEASES OF THE UTERINE APPENDAGES

421. Under the term uterine appendages are included the structures contained between the layers of the broad ligaments, along with the ovary which is attached to the posterior surface. The Fallopian tube may become blocked and subsequently dilated by inflammation of its lining membrane—Salpingitis. This condition is generally the result of the spreading inwards of gonorrhœal, or septic inflammation. The secretion of the tubes becomes increased in quantity, especially during the

Description of Fig. 216.

FIG. 216.—Section of chorion epithelioma, stained with alum hæmatein and van Gieson's stain. ($\times 50$.)

- a.* Plasmodial cells around a villus and *a'* in the tumour mass.
- b.b'*. Cells derived from Langhans' glycogen-bearing cells.
- c.* Comparatively normal villus.
- d.d'*. Large wandering or perforating cells.
- e.* Muscular tissue of uterine wall.
- f.f'*. Small hæmorrhages and collection of fibrin.
- g.* Mass of fibrin.

menstrual periods, and may become altered in character. The fimbriated end often becomes glued to the ovary, and should obstruction of the lumen occur at any other point the secretion accumulates in the intermediatè portion, and more or less dilatation results. The fluid contained in such dilatations varies from serum to pus. Sometimes constriction occurs at more than one place, giving rise to two or more cyst cavities. The tubes are sometimes very much thickened, though not dilated, the thickening being due to inflammatory processes either of their walls or of the peritoneal covering, or of both.

Elongation of the tube usually occurs along with the growth of parovarian tumours, or of uterine fibroids which have opened out the broad ligaments. Gestation may take place in a tube, in which case rupture of the tube often occurs early in the pregnancy. Gestation may terminate by tubal abortion or by the formation of a tubal mole; in rare cases it may continue in the unruptured tube until the fœtus is viable, or, after rupture of the tube, a secondary gestatic sac may be formed, within which development may proceed in the same manner.

Other cysts besides those of the tubes develop between the layers of the broad ligament, the Parovarium or organ of Rosenmüller being their usual starting-point. Such cysts frequently attain great size, coming to resemble ovarian tumours. The distinction between them and ovarian tumours may be made out either by the character of their contained fluid; by finding the ovary—probably flattened and atrophied—at some part of the wall; by the fact of their being monolocular; or by their being covered by peritoneum—derived from the broad ligament—ovarian cysts, like the ovary itself, being devoid of peritoneal covering.

THE OVARIES

422. On examining a section of the ovary, there is noticed an outer investing layer, the tunica albuginea, a central vascular and fibrous layer with large vessels entering it from the hilus, and between the two a stroma of fibrous tissue with a few muscle cells; thickly scattered through this are the Graafian follicles in all stages of development and retrogression. Usually a corpus luteum may be found. The Graafian follicles are small cyst-like cavities lined with epithelium, which is heaped up at one part of the circumference around one cell of special size, the ovum. The origin of the Graafian follicles is of sufficient importance, as bearing on the development of ovarian

tumours, to warrant a brief reference to the conflicting theories—those of Waldeyer and of Foulis. Both observers are agreed that the ovum was originally an epithelial cell on the surface of the ovary, which became embedded in the stroma of the organ. Waldeyer holds that the epithelial cells of the Graafian follicle were also at one time cells of the surface, while Foulis regards them as being derived from the connective tissue of the ovary as a result of the irritation set up by the presence of the ovum; as being, in fact, granulation cells which have become epithelial in character.

423. *Tubercle and cancer* occur in the ovary—usually secondarily, sometimes primarily. Cancer, when secondary, affects both ovaries.



FIG. 217.—Sarcomatous degeneration of ovarian cystic tumour, showing infiltration of the stroma and filling up of small cysts with round cells. Stained with logwood. ($\times 50$.)

When primary, one alone may be affected, but the tumour rarely attains any considerable size. What is spoken of as malignant ovarian tumour is not cancer of the ovary, as will be explained presently.

424. *Inflammation and cirrhosis of the ovary.*—The ovaries may be found in any stage of inflammation, from the initial congestive stage to that of the formation of new fibrous tissue upon the one hand, or suppuration upon the other. Abscess formation—a rare occurrence—may follow tuberculous, gonorrhoeal, or septic infection, and possibly

other forms of inflammation. In such cases the ovary becomes adherent—in the pelvis or to the abdominal wall—and the relationship of parts becomes greatly altered.

425. Cystic disease of the ovaries.—It is quite common to find one or more cysts in the ovaries, due to abortive maturation of a Graafian follicle, but this condition must not be confused with the multiple cystic formation which occasions the growth of “ovarian tumours.” Such cystic ovaries are almost invariably found where large, rapidly growing, or bleeding uterine fibroids are present.

The multiple ovarian cystic tumour will be described in the chapter on Tumours (§ 449); here it is only necessary to notice the changes which may occur in it. Sometimes acute inflammation of the interior of one or more of the cysts takes place, and the contents may become purulent, thus occasioning one form of abscess of the ovary. Sarcomatous change may occur in the wall of an ovarian cyst starting in the sub-epithelial connective tissue. Cancerous change may also occur, but is probably less common. Large solid encysted carcinomatous growths may occur in the ovary, secondary to carcinoma of the liver or of some part of the alimentary canal. Primary carcinoma may also occur in the ovary apart altogether from the presence of cystic disease; but ovarian cancer is more often secondary than primary. Ascites is very commonly associated with malignant ovarian growths.

Dermoid cysts of the ovary are also described (§ 451).

DISEASES OF THE VAGINA AND VULVA

426. The mucous membrane of the vagina is frequently the seat of inflammatory affections, and the changes it undergoes differ in no respect from those occurring in other similar structures. Occasionally small collections of gas are found in the submucous connective tissue meshes, the condition being then called emphysematous vaginitis. In old women a form of vaginitis occurs in which the walls become thinned, dry, and parchment-like. Malignant disease of the cervix frequently spreads to the vagina; occasionally the latter is the seat of primary disease. Cicatricial contractions, especially of the upper part of the canal, are often found as the result of tears, which may have occurred during parturition.

The vulva is the seat of many of the ordinary skin affections, such

as eczema, as also of the manifestations of syphilis in its various stages. The natural moist condition of the vulva greatly favours the occurrence of condylomata or warts when syphilis or gonorrhœa are



FIG. 218.—Section of a hypertrophic growth from the neighbourhood of the hymen in a case of lupus vulvæ. Stained with logwood. ($\times 50$.)

- a.* Thickened layer of epithelium.
- b.* Proliferating mass passing into the corium.
- c.* Proliferating mass seen in transverse section, both surrounded by proliferating connective tissue cells.
- d.* Vascular nodule (mass of connective tissue cells around vessels).
- e.* Vascular nodule without vessels.
- f.* Mass of disintegrated tissue at the margin of the lupus ulcer.
- g.g.* Hemorrhages.

The blood vessels, lymphatics, and diffuse infiltration are all well seen.

present. In cases of diabetes, where there has been pruritus vulvæ or where that condition has been present from other causes, the external genitals are often found swollen and scratched, and some-

times covered with eczematous eruptions. These changes are purely the result of the scratching, and are not the cause of the pruritus, which affection may be present, even to a most intense degree, without any pathological change being evident. Occasionally there are found, studding the neighbourhood of the hymen, the vulva, and adjoining parts, a number of small rounded red spots of apparent ulceration, with numerous cicatrices, the remains of previously affected parts. This condition has been called lupoid disease, but its true pathology is not yet fully understood. Certainly there is not complete loss of epithelium, and, clinically, we know that while in some instances these spots are extremely sensitive, in other, to all appearances undistinguishable cases, no special sensitiveness exists. Clinically, also, we know that it is a most intractable disease to treat, as it constantly recurs even after complete destruction of all existing spots.

427. *True lupus* occurs in the vulvo-anal region, and is extremely apt to be mistaken for a syphilitic manifestation. It affects both the parts covered by skin and those covered by mucous membrane, and cases have been described in which the process was entirely limited to the vagina. Very probably the so-called "corroding" or "rodent" ulcer of the cervix uteri is of lupoid nature. All the ordinary forms of the disease have been found in this neighbourhood, but the most commonly occurring variety is that which is accompanied by hypertrophies and ulcerations. The hypertrophies are of already existing parts, as of the labia majora or minora, or of the hymen, or they occur as outgrowths, usually finger- or club-shaped, projecting from the affected surfaces. The disease seems to consist in an infiltration of the connective tissue, with granulation cells, which make a feeble attempt to organise into fibrous tissue, but which usually become so crowded together that they interfere with their own nutrition, and lead to ulceration. Along with this there is proliferation of the epithelial covering.

In Fig. 218 the changes are seen to be very similar to those met with in lupus of the skin. This represents a section made across one of the hypertrophic growths taken from such a case. The portion was about the size of the last joint of the little finger, and was completely surrounded by a thick layer of epithelium, presenting a smooth surface externally, but with an irregular deep surface, from which, here and there, branched prolongations passed into the substance of the mass.

The central portion was made up of a meshwork of connective tissue in all stages of development, in which there were numerous spaces, some distended with blood, others containing granular material, probably coagulated lymph, while others, especially those near the surface, resembled gland ducts, and were lined by regular epithelium. Immediately under the epithelial investing layer, notably where the prolongations passed inwards, there were numerous deeply stained round bodies, which under a high power were seen to be nuclei. These were grouped around the openings above mentioned, and were also sparingly scattered through the connective tissue. The cells, of which these were the nuclei, were very delicately stained, and some of them were of considerable size, and contained more than one nucleus; it was from these cells, apparently, that the connective tissue was developed. They were very similar to those met with as endothelial plates in gummata, tubercle follicles, and similar growths. Sections made from other parts taken from the same case showed a similar condition in evidently a further stage of its history, the cells being present in greater numbers; in one of the specimens they were so crowded together that they appear to have led to breaking down and ulceration. A section made from a hard wart-like structure over the mons veneris had all the characteristics of an ordinary wart or papilloma, with, in addition, a few cells similar to those existing in the other specimens, sparingly scattered through the connective tissue.

428. Malignant growths of an epitheliomatous type may occur in any part of the vulva, but they are especially apt to affect the clitoris. The glands of Duvernay, situated laterally beneath the lower end of the vagina, are frequently the seat of acute inflammation and supuration, when they bulge into the labia; if they burst, sinuses are left. The canal of Nuck—a developmental prolongation of the peritoneum around the round ligament into the labium majus—may, very rarely, remain as a closed sac, and give rise to a retention cyst in that locality.

CHAPTER XIV

TUMOURS

429. In examining tumours, it should always be borne in mind that no new or peculiar structural elements are imported into, or developed in, the body, with which to build them up. The tissues of which each tumour is composed have their homologues in some part of the body, at some stage, at least, of its development. Hence it is sometimes an extremely difficult matter to determine, merely by microscopical examination, whether a tissue is taken from a tumour or not. One often hears of "cancer cells." It is an absolute impossibility to say with certainty from microscopic examination that the epithelial cells found in "cancer juice" are "cancer cells." The observer is assisted by a microscopic examination, and the evidence so gained, along with that derived from other sources, may enable him to arrive at a definite conclusion ; but a mere examination of so-called cancer cells will not enable the observer to say that they are anything more than epithelial cells.

In the same way it is often impossible to distinguish granulation tissue from round-celled or mixed sarcoma tissue ; both are made up of connective tissue cells in an early stage of development, and of embryonic blood vessels.

It behoves the observer, therefore, to take great care that he is not led to search for distinctive or characteristic tumour elements. His great aim should be to determine the position, proportion, stage of development, and arrangement of the various tissue elements, which together will give him far more certain indications as to the nature of the growth than can be derived from any amount of study of the mere form of the individual elements.

Definition.—A tumour or neoplasm consists of an atypical new growth of tissue, which has an existence of its own quite irrespective of the needs of the organ or tissue in which it grows, and which is

independent of all surrounding local conditions except as regards its nutrition. It has an active vegetative existence and is always growing, but it never takes on any reparative or functional activity; though it never retrogresses in type, it never attains any special and complete developmental form, and ultimately it may undergo fatty or caseous degeneration, calcification, or change of type of tissue. Such a growth is always composed of tissue differing, though sometimes very slightly, from that in which it grows. Even when the tissue of a new growth is of the same class of tissue as that in which it arises, it is never precisely the same or at the same stage of development.

Moreover, the structure is essentially permanent in character, though seldom perfectly typical. Any kind of tissue may be reproduced in it, but the connective tissue, so characteristic of inflammatory hyperplasia, here, as a rule, acts merely as a framework, and is not an essential part of the tumour.

It may be freely supplied with nerves, lymphatics, and blood vessels from the surrounding parts.

In other words, a tumour may be looked upon as a superadded growth of various tissues, either in the adult or in the young child, developing abnormally. Its growth is not defined by an obvious limit, as is the growth of normal tissues. It never reaches a point at which growth ceases, though considerable areas may undergo involution changes.

By its presence it may act mechanically by pressure on nerves, blood vessels, or vital organs, or it may exert a constitutional influence—cachexia—especially in those cases of malignant tumour where there is ulceration or any great discharge.

Tumours may, for the sake of convenience, be considered in three large groups, which may be taken in the following order:—

I. Histioid tumours are tumours composed of tissues which deviate but slightly, if at all, from those of which a healthy body is built up. These tumours may be divided into two groups, (*a*) Simple Histioid Tumours, mesoblastic in their origin, and, of course, mainly composed of some form of connective tissue; and (*b*) Compound Histioid Tumours, or tumours composed of epithelial and connective tissues which do not depart in their arrangement from normally developed structure.

II. Sarcomatous tumours are composed of tissues more or less embryonic in type, in which there may be some attempt at higher development—which attempt, however, *is always abortive or incomplete*. These are also mesoblastic, and are therefore composed of tissues, *imperfectly developed*, of the connective type.

III. Cancerous tumours are those in which some or all of the tissue elements may be present in excessive or erratic form. There is a loss of balance between the tissues, which are derived from mesoblast and hypoblast or epiblast.

HISTIOID TUMOURS

430. *General characters*.—These tumours all grow comparatively slowly. They are usually single, rounded (rarely flattened), or lobulated, and are surrounded by a fibrous capsule which, like the pseudo-cyst of the hydatid cyst, is formed of fibrous tissue, due to proliferation of the connective tissue cells, the result of the chronic local inflammation set up by the presence of the tumour itself. They are non-malignant, and give rise to no inconvenience or injury, except by their weight and mechanical pressure. On section, fibrous bands or trabeculae can be seen passing in from the capsule, between the individual lobules; along these bands and in the capsule run the blood vessels.

They are liable to undergo certain degenerative processes, of which fatty degeneration and calcification, ulceration, colloid degeneration of the cells, and mucoid degeneration of the fibrous or connective tissue are the more important. Hæmorrhages frequently occur in the softer forms, and inflammatory changes may be set up by mechanical injury or by the action of irritant chemical substances or putrefactive products.

(a) SIMPLE HISTIOID TUMOURS

MYXOMA

431. A myxoma is a tumour made up of delicate branching connective tissue cells embedded in a mucoid matrix (myxomatous tissue) like that found in the vitreous humour of the adult, and is non-malignant, although it is composed of a tissue which in many respects is embryonic, such as is met with in the developing embryo

as the subcutaneous tissue, from which fatty tissue is later developed. Wharton's jelly of the umbilical cord and young connective tissue have a similar structure. Myxomatous degeneration of the villi of the chorion is spoken of as a form of multiple myxoma. In this case there are rounded or pear-shaped masses of myxomatous tissue, held together by portions of the healthy villi. Myxomas are also found in the submucous tissue as nasal polypi, in the subcutaneous and other connective tissue, in the intermuscular septa, between the bundles of nerves, in periosteum, and in subserous fat. In rare cases a myxoma may grow on the umbilical cord.

Naked-eye appearances.—It grows slowly, and does not often reach any very great size, though occasionally it may do so. It is lobulated, and is surrounded by a delicate capsule, from which trabeculae run into the tumour mass. On section, the tissue between the trabeculae, which projects beyond them, is clear and gelatinous, and is often compared to a mass of boiled tapioca. Running along the trabeculae, and into this gelatinous substance, are small blood vessels, seen as thin red lines. Usually some of these have given way, as the mucous tissue does not afford them an efficient support, and small hæmorrhages, red, brown, or yellow, according to their age, may be seen in the clear mass. Examine some of the viscid fluid scraped from the surface ($\times 300$); it contains a number of coloured blood corpuscles, and some nucleated cells with one or two nuclei and some with several branching processes. Unless these cells are stained, it is very difficult to distinguish them. Immerse a small piece of the tumour in acetic acid or alcohol, either of which immediately precipitates the mucin between the branching cells, and renders the section opaque.

Harden (§ 63, 64, or 65), cut (§ 94 *et seq.*), stain (§§ 103, 110 (*b*), 132), and mount (§§ 193 and 199).

($\times 50$).—Under the epithelial layer, with its columnar and "goblet" mucous cells, comes the tumour tissue, proper. Between trabeculae, which in most cases are more fibrous, but which may be composed of very cellular material, and in which may be seen running small blood vessels, is the true myxomatous tissue. This is made up of a number of branching cells, each having one or more deeply stained nuclei, around which is a large quantity of protoplasm; between the individual cells are spaces, in the fresh condition occupied by mucin, with here and there small groups of blood corpuscles (small

hæmorrhages), whilst rounded cells, sometimes in fairly large numbers, may also be seen.

($\times 200$ or 300).—Beneath the epithelial layer, the fibro-cellular trabeculae are seen gradually merging into the myxomatous structure.

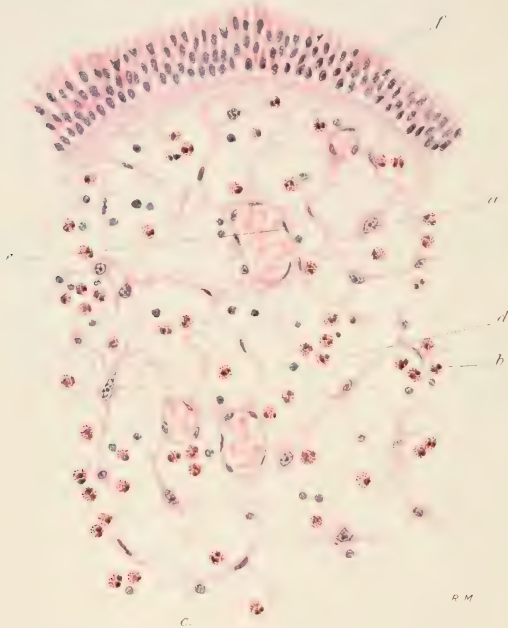


FIG. 219.—Drawing of myxoma. Section stained with alum hæmatein and eosin. ($\times 200$.)

- a.* Branching myxomatous cell with single nucleus.
- b.* Rounded cells with double nuclei.
- c.* Nucleus of lymphocyte.
- d.* Intercellular spaces containing mucin.
- e.* Small blood vessels, imperfectly supported.
- f.* Columnar and "goblet" cell epithelium of mucous surface.

Note the granularity of the protoplasm of the branching cells, the number and ramifications of the processes, and the intercellular spaces, in which may now be made out a number of small round cells—polymorpho-nuclear leucocytes, lymphocytes, and young connective

tissue cells. Any blood corpuscles which may have escaped from the blood-vessels are in various stages of disintegration. In the breast, the myxomatous tissue may extend between the acini of the gland, whilst in some specimens it is found to encroach on the acini, growing into them and distending them, as granulation tissue does when it forms the so-called cystic sarcoma.

Varieties of Myxoma

(1) Pure myxoma: (*a*) Hyaline form, composed of an exceedingly translucent substance, with few round cells between the branching cells; (*b*) Medullary form, which is more opaque from the presence of a greater number of the small round cells.

(2) Myxoma containing a quantity of elastic tissue.

(3) Lipomatous myxoma, in which some of the branching cells are distended with droplets of fat.

(4) Cystic myxoma, formed by the softening of certain portions of the tumour.

Degenerative Changes

(1) Hæmorrhagic.

(2) Muroid and colloid degeneration of the cells.

(3) Inflammation, which may become gangrenous and ulcerative,—especially where the polypoid tumour is on a free surface, and is therefore exposed to mechanical injury.

GLIOMA

432. Two forms of glioma are usually described, one of which appears to be simply a form of small round-celled sarcoma, a malignant tumour sometimes found in the retina. The true glioma is a non-malignant tumour composed of connective tissue similar to that found in the nerve centres. It occurs in the brain and spinal cord, especially around old cysts and in cases of syringomyelia, more frequently in the former than in the latter, and in children than in adults.

Naked-eye appearances.—It is a gelatinous-looking mass, evidently of slow growth, which gradually replaces the nerve tissue, into which it merges at its margins. On section it has a grey, translucent, or a greyish or dark red colour, according to its vascularity. It may be distinguished from the small round-celled sarcoma, which frequently occurs in the same positions, by the fact that even in the form where

hæmorrhages occur (the dark vascular form) and where we have softening in the centre, the surrounding substance is distinctly firmer.

Harden (§ 62 or 63) and stain (§ 106), half clear up (§ 394), to bring out the processes of the Deiters' or neuroglia cells distinctly, or stain a section (§ 102 or 103) and of this tease out a small fragment.

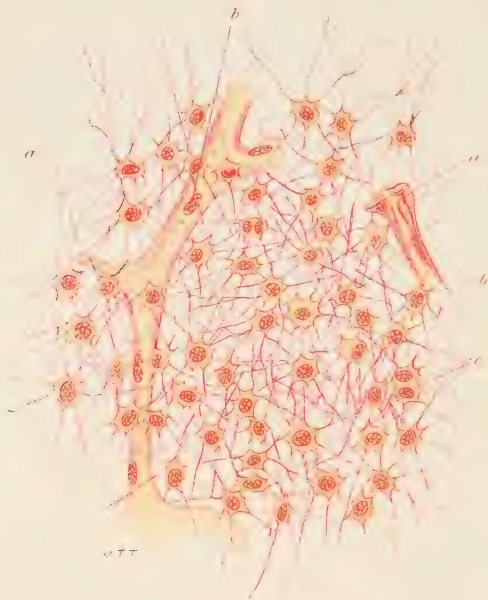


FIG. 220.—Glioma taken from the brain. Section stained with carmine, and half cleared up. ($\times 600$.)

- a.* Capillary blood vessels.
- b.* Nuclei, with intranuclear plexus well seen.
- c.* Neuroglia cells, or Deiters' cells, with nuclei and long branching processes.

($\times 50$).—The tumour is composed of neuroglia cells, the nuclei of which are very distinctly seen grouped round the small blood vessels (of which there may be local or general dilatation) running through the mass. Between them is a tissue, the structure of which cannot be determined under this power.

($\times 300$).—Examine a few of the cells in the teased-out specimen. They consist of granular-looking protoplasm, embedded in which are one or two rounded or ovoid nuclei. From the main body of the cell run out branching processes, very like those met with in myxoma. In the half cleared-up section, the capillary blood vessel with its endothelial plates, and the branching cells with their large nuclei, and long, delicate, and anastomosing processes, stand out distinctly. If a section be stained and mounted by any of the ordinary methods, the nuclei are readily demonstrated, but the tissue between appears to be composed simply of felted fibrils seen as a granular mass, where the transverse sections of the fibrils are numerous. In various chronic inflammatory conditions in the spinal cord, medulla oblongata, and brain, this gliomatous tissue may be greatly increased in amount, and a similar tissue is found in large quantities in the dense walls of old cysts in the brain.

Degenerative changes.—Hæmorrhagic (as in myxoma), fatty, caseous, or simple softening.

LIPOMA, OR FATTY TUMOUR

433. This tumour is composed of fatty or adipose tissue, and usually grows in connection with pre-existing fat. It occurs most commonly in the subcutaneous tissue, especially in such parts as are subjected to pressure, as on the shoulders or buttocks, also in the abdominal wall, in the breast, and as the arborescent lipomas of the synovial fringes of joints. Sometimes, however, it is found in tissues which, normally, do not contain fat, as in the dura mater, in the sub-mucous tissue of the intestine, and rarely in the liver and heart, between muscles and in bone. It is of slow growth, and may be single or multiple.

Naked-eye appearances.—The lipoma is usually rounded and lobulated or flattened, or it may be pedunculated when it occurs in the fatty synovial fringes or enlarged appendices epiploicæ. Its size varies from that of a pea up to a growth of many pounds in weight. It has a well-formed fibrous capsule, from which septa run in and cut the fatty mass into a series of lobules, it may easily be shelled out from this capsule. On section the surface presents the appearance of a mass of yellow fatty tissue, through which run white and glistening fibrous septa, containing the blood vessels; these blood vessels supply the

tumour tissue, which is much softer and more plastic than ordinary fatty tissue, with blood.

Harden (§ 61, 63, or 65) and stain (§§ 102, 103, or 110 (*b*), and 132).

($\times 50$).—Note that the tissue resembles ordinary adipose tissue, but that the fat cells are rather larger, that the tissue is extremely vascular, and that at certain points there are, in addition to the fully-



FIG. 221.—Drawing of lipoma. Stained with logwood and mounted in Canada balsam. ($\times 250$.)

n. Nucleus of fat cell.

n.c.t. Collection of connective tissue nuclei (cells not infiltrated with fat).

p. Thin film of protoplasm surrounding fat globule.

m. Remains of bands of fibrous tissue.

developed connective tissue cells distended with fat, numerous embryonic cells, in which the process of fatty infiltration is as yet incomplete. These latter occur in isolated groups as small, deeply stained cells in which there is frequently not a single droplet of fat.

($\times 300$).—The swollen connective tissue cell, infiltrated or loaded with fat, is seen with its nucleus pushed into an angle, the protoplasm

of the cell forming a thin film or coat around the fatty globule. Sometimes these cells contain fat crystals, and usually they are so closely packed together that they assume a polygonal form. Under this power a number of the uninfiltrated cells are seen to be myxomatous (§ 431).

Varieties of lipoma—(1) Pure lipoma—the form described.

(2) Myxomatous lipoma, in which the branching myxomatous cells, with intercellular mucoid substance, are very numerous.

(3) Fibrous lipoma, in which the fibrous trabeculae are well developed and very numerous.

(4) Osseous lipoma, described by Cornil and Ranvier, in which the trabeculae are osseous.

(5) Erectile lipomas, principally met with as very vascular polypoid growths on serous and mucous surfaces.

Degenerative changes.—The tumour may undergo—(1) Myxomatous degeneration; (2) molecular softening, when it becomes opaque and putty-like; (3) calcareous degeneration; (4) inflammation and ulceration, where young connective tissue cells are formed more rapidly than they are filled with fat.

FIBROMA

434. The fibroma is a tumour composed of fibrous tissue, and, as a rule, grows where fibrous tissue already exists; it is of comparatively slow growth, and is non-malignant. It occurs most commonly in the subcutaneous and submucous tissues; in the upper and posterior part of the pharynx (then probably growing from the periosteum of the basilar process); in fasciae, and in the interfascicular tissue of nerves, especially of the skin; in the mamma and ovary; in the uterus; as small, firm, rounded masses, about the size of a pin's head, or larger, in the centre of a pyramid of the kidney; as keloid growths in scars; and as the so-called loose cartilages of the knee-joint.

There are two forms of fibroma, fasciculated and lamellar, of which the fasciculated is perhaps the more characteristic.

Naked-eye appearances.—It is usually met with as a firm, dry, glistening, white or brownish, not very vascular tumour. It may be rounded or lobulated, has a capsule, and on section presents a peculiar watered silk appearance, or it may be not so firm, when it is somewhat pinker and more gelatinous looking. Notice the lobular arrangement; each lobule is composed of a number of concentric layers of fibrous tissue; they are softer towards their centre, at which point they seem

to grow; between them is a quantity of looser connective tissue, in which run numerous blood vessels. When the cut surface is scraped, small fragments and but little fluid are removed. Treat one of these fragments with acetic acid and examine ($\times 300$). It is seen to be composed of small bundles of connective tissue, which swell up, become



FIG. 222.—Drawing of a hard fibroma. Stained in logwood, and mounted in Canada balsam. ($\times 50$.)

f.t. Bands of well-developed fibrous tissue, in which are few nuclei.

n.c. Intervals between the fibrous bands, in which the tissue is more cellular, the strands of formed tissue running obliquely, with well-marked nuclei between them.

gelatinous or homogeneous, and allow one to see the connective tissue cells as branching nucleated specks of protoplasm.

Harden (§§ 60–63) and stain (§§ 102, 103, or 110 (*b*), and 132).

($\times 50$).—Stained with picro-carmin or van Gieson's stain, the tissue throughout takes on a beautiful pink (a reaction very characteristic of fibrous tissue). The fibrous tissue has different arrangements in different parts of the tumour, but it is in great part disposed in

bundles, which (1) run in various directions, or (2) are arranged concentrically, or (3) have a peculiar feather-like or ladder-like arrangement. In the last form there are dense pink bundles, which may be said to run longitudinally, whilst running off at various acute angles are more

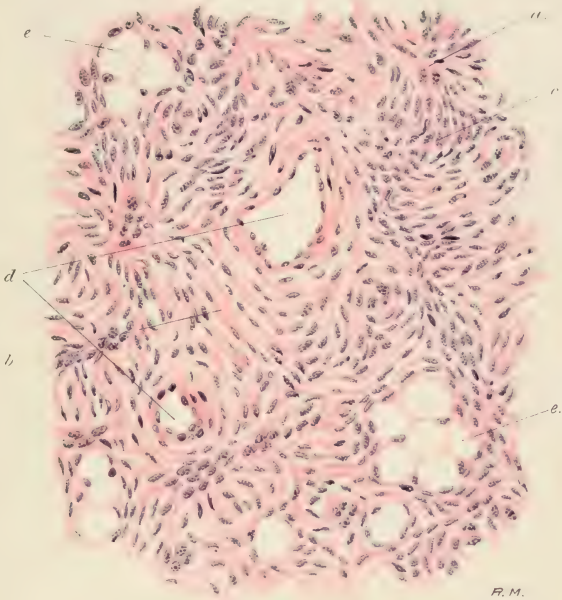


FIG. 223. Section of a soft fibroma from the subcutaneous tissue of the hand. Stained with alum hæmatein and eosin. ($\times 200$.)

- a. Fibroblasts arranged in irregular "vortices," groups running in lines with other groups running at right angles to them.
- b. Older less cellular portion.
- c. More rapidly growing cellular portion.
- d. Vascular channels lined with endothelium.
- e. Fatty tissue.

delicate strands. In the dense longitudinal bundles there are few cells; in and between the more delicate transverse strands numerous nuclei are seen in the cells. Whatever be the arrangement of the bundles, the cells—small, round, elongated, or branching—are always

most numerous in the more open tissue, when we have what is known as a soft fibroma. There are never any yellow elastic fibres present. Observe that the blood vessels running in the capsule and trabeculae are all fully developed, but are not very numerous.

In a molluscum fibrosum, where there is a kind of oedema of the fibrous tissue—a distension with fluid of the spaces between the fibres—the arrangement of both fibres and cells is very easily seen.

($\times 300$).—Look for the fibrous bundles, between which are branched cells, the processes of which clasp these bundles. Observe how scanty are the cells in the denser fibrous bands, and how numerous they are in the soft open parts of the tumour, especially between the transverse bars of the ladder. Examine the cells carefully; some are embryonic cells, nearly all nucleus; others are surrounded by a quantity of protoplasm; others are elongated, and the formed material around them is becoming fibrillated; others again have several nuclei; and some have well-developed branching processes. In fact, a young or growing fibroma is composed of the purest form of fibrous tissue, and is one of the best structures in which to study its development.

Degenerations.—(1) Serous infiltration, as in the molluscum fibrosum; (2) mucoid degeneration of the fibres; (3) fatty degeneration, especially in fibromas of syphilitic origin (Cornil and Ranvier); and (4) calcification. The two changes last named occur near the centre of the nodules, or away from the blood vessels. Inflammatory changes and new cell formation are sometimes set up, especially when the tumour is exposed to mechanical injury.

THE LAMELLAR FIBROMA OR FLAT FIBROMA.

435. Flat fibromas can scarcely be looked upon as true fibromas. They are formed rather by a thickening of lamellated tissue—the result of a chronic inflammatory process on a serous surface. They are met with as flattened, hard cartilaginous masses, which vary considerably in size and shape. They occur on the outer surface of the spleen and liver (especially after abdominal dropsy); on the pleura, or in the subpleural tissue in old people; in stone-masons' lung and on the inner surface of blood vessels in certain conditions. They are usually yellow and translucent, but they may be pigmented; they are cartilaginous in consistence, and are cut with difficulty.

Harden and stain as in § 434.

($\times 50$).—The structure is essentially that of corneal tissue, or of the inner lining of vessels—a series of laminae of fibrillated tissue, between which are flattened cells.

($\times 300$).—These flat cells are only flattened, branching connective tissue cells, seen in profile. In order that these cells may be examined fully, a small fragment must be treated with acetic acid, then stained with carmine (§ 106), and carefully teased out.

CHONDROMA

436. A chondroma is a tumour composed of cartilaginous tissue. It grows, usually, in the periosteum of bones (especially at the ends of the metacarpal bones and on the phalanges of the fingers and toes); in the bones themselves; in the parotid and other salivary glands; and in the testicle, skin, lung, and mamma, and sometimes from the cartilages of the ribs or of the larynx.

Naked-eye appearances.—Such tumours are usually met with as multiple growths, firm and elastic, though in some cases, owing to mucoid degeneration, they may be soft and even gelatinous; they may be either rounded or lobulated, and are surrounded by a fibrous capsule, with fibrous bands separating the lobules from one another. On section the tumour “cuts” with the peculiar creak of cartilage, but when calcification has set in, there is also a gritty feeling. Running across the section are white glistening fibrous trabeculae, between which the cartilage, with its translucent pearly appearance with a bluish or pink tinge, is seen.

Harden (§ 60), stain (§§ 102, 103, or 110 (*b*), and 132), and mount (§§ 195 or 193 and 199).

($\times 50$).—The capsule of the tumour is seen as a pink fibrous band, at one margin of the section. From it a series of fibrous trabeculae, in which run small vessels, extend between the masses of cartilage. Rapidly developing hyaline cartilage cells, with well-formed cartilage capsules, are seen; the capsules have disappeared from some of the cells, which appear as branching cells sending their processes in all directions into the matrix, which here is soft and mucoid, and takes on a very delicate stain. Near the centre of each lobule where calcification is beginning, the tissue is green, and much less translucent. At the margin of the calcified part granules of calcareous material may be seen embedded in the matrix, whilst in some few cases the cal-

careous particles appear to have found their way into the cartilage capsules.

($\times 300$).—The greater part of the tumour is composed of hyaline cartilage, made up of encapsuled and proliferating cells in a matrix, which in this case is not fibrillated. The branching cells in the mucoid matrix, and the fibrous capsule and trabeculae, with the well-developed

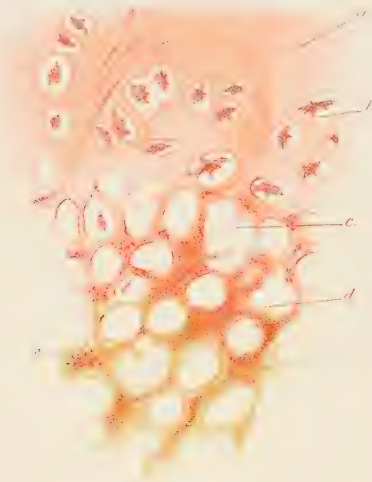


FIG. 224.—Section of a chondroma taken from the parotid gland.
Stained with picro-carmin. ($\times 200$.)

- a.* Homogeneous cartilaginous matrix, in which are embedded
- b.* Branching cartilage cells.
- c.* Spaces from which cells have disappeared.
- d.* Granular matrix (calcification just beginning).
- e.* More advanced calcification.

blood vessels, and the yellowish-green part, with the highly refractile calcareous particles infiltrating the matrix around the distended capsules, are all well seen.

In another section of a parotid tumour of softer consistence growing more rapidly and prepared as above, the tissue was composed almost entirely of branching cells embedded in a mucoid matrix, with proliferating gland structure running through it. The epithelium of the

gland acini and ducts takes part in the increased activity of the surrounding tissues, and grows so rapidly that it forms solid-looking columns or masses, which intersect the myxochondromatous tissue in all directions. This form of parotid tumour is spoken of as the myxochondro-adenoma.

MYXOCHONDROMA

437. Certain cartilaginous tumours are much softer and more gelatinous than the form last described; they grow with extreme



FIG. 225.—Section of myxochondroma. Stained with picrocarmine. ($\times 200$ —*circa*.)

- a.* Fibrous capsule from which run in
- b.* Trabeculae.
- c.* Mucoid matrix, in which are embedded
- d.* Embryonic cartilage cells, proliferating rapidly, and of various shapes.

rapidity, and frequently give rise to similar growths in other parts. In the case from which the section described was taken, the tumour grew from the periosteum of the scapula, increased very rapidly in size, and gave rise to secondary growths of a similar nature in the lung, in the branches of the pulmonary artery. It was a soft lobulated tumour, composed of a brown gelatinous material surrounded by a very vascular fibrous capsule. Prepare as in § 431.

($\times 50$).—The fibrous capsule and trabeculae are readily seen, and running in them are well-formed blood vessels. Near the trabeculae

the cells are somewhat flattened, and have a comparatively regular arrangement. Towards the centre of the mass are large cells, very irregular in shape, having long processes, and often two, three, or four nuclei and nucleoli. Between these huge cells, which are compared by Ranvier to the cells of the cartilage found in cephalopods, the matrix is somewhat fibrillated near the periphery, but mucoid towards the centre. Towards the periphery greenish masses (coloured blood corpuscles) may be seen.

($\times 300$).—Note the forms of the cells and the structure of the matrix.

All varieties of cartilage between the white fibro- and hyaline-forms may be found in these chondromas. They may be combined with an adenomatous growth. Then there are certain malignant forms, the chondrosarcoma, osteochondroma, also a malignant form in which there is a formation of imperfect bone and osteoid chondroma consisting simply of calcifying cartilage; this also is usually malignant.

Degenerations.—(1) Mucoid softening of the matrix; (2) calcification of the matrix; (3) true bone formation.

OSTEOMA

438. Osteomas, or bony tumours, occur chiefly at the point of junction between a bone and its cartilage; they also grow in fasciæ, periosteum, tendons and ligaments, within bones, in the pia mater and dura mater, in the choroid and sclerotic coats of the eye, at the apices of the lungs, in the skin and mucous membranes, and sometimes even in the penis and in muscular tissue. These outgrowths of bone are classified according to their position into *exostoses*, or those growing from the surface of a bone, and *enostoses*, or those growing in its interior. A more natural classification is that in which they are arranged according to their structure, as (1) eburnated, (2) compact, and (3) spongy osteoma.

(1) The *eburnated osteoma* occurs most frequently as a syphilitic growth from the inner table of the skull. It is extremely hard, and is often multiple and symmetrical.

Prepare (§ 79 or 81), stain (§§ 102, 103, 104, or 110 (*b*), and 132), and mount (§ 195 or 199).

On section notice that the dense bony structure is composed of lamellæ, which are arranged parallel to the surface of the tumour

(Virchow)—*i.e.* they are arranged in convex layers, which follow, more or less closely, the free outline of the tumour. In the lamellæ there are no blood vessels and no Haversian canals: but, according to Cornil and Ranvier, there are canaliculi, similar to those found in the "cement" of a tooth, which run towards the surface.

The *compact osteoma* is composed of ordinary compact bone, similar to that found near the surface of a long bone. It is met with as a nodular growth, usually beneath or in the periosteum, especially of the long bones: but it may be found growing in the substance of a bone, in the meninges of the brain, in the choroid coat of the eye, in the pericardium, in the skin, around glands, in the apices of tuberculous lungs, even in the nerve centres; also in tendons, in intermuscular septa, and in other positions where new fibrous tissue formations occur. Make a vertical section through the growth with a saw, and examine with a low power lens, when it will be observed that it differs from the eburnated osteoma in that the vessels and Haversian canals run at right angles to the long axis of the bone.

Prepare (§ 75 *et seq.*) and stain and mount as above.

($\times 50$).—Notice that the structure is essentially that of compact bone, that the vessels run in the Haversian canals at right angles to the long axis of the bone, that there is a periosteal fibrous covering, with a layer of small round cells—osteoblasts—and young bone formation beneath. Around the Haversian canals regular Haversian systems may be readily distinguished.

The *spongy osteoma* differs from the compact form only in the fact that the trabeculæ are much thinner and not so numerous; that the medulla is usually more embryonic in character, and appears to the naked eye as a gelatinous mass; in some cases, however, it is almost fibroid. The whole tumour is essentially like the spongy tissue of which the ends of long bones and the bodies of the shorter bones are composed.

($\times 50$).—Treat as for compact osteoma. A few fat cells can usually be observed amongst the small round cells which compose the main mass of the medullary tissue.

Odontoma composed of dentine is sometimes found on the root, neck, or crown of a tooth. A true bony tumour may, however, grow from the cement of the tooth.

MYOMA

439. Myoma is a tumour composed of muscular tissue of one of two forms.

(1) That composed of striped muscle fibre is an exceedingly rare form, and probably is met with only as a result of the higher development of sarcomatous tissue, in which case the muscle is imperfectly developed, and never gets beyond an embryonic stage.

(2) In the ordinary myoma or leio-myoma there is a formation of well-developed non-striped muscle fibres. This form is met with so much more frequently in the uterus than in any other position, that it has been named the "uterine fibroid." It may, however, occur in any position in which non-striped muscle is normally present, as in the gastro-intestinal tract, where it is seen as a polypoid growth; in the wall of the bladder; in the prostate in old men; in the skin, especially of the scrotum; and in the kidney, where it is developed near the apices of the papillæ. Under certain conditions it may assume a rapidly growing form and take on a sarcomatous character—"myoma sarcomatodes."

Naked-eye appearances.—The typical leio-myoma may be small and rounded, or it may grow to an enormous size, when it is usually lobulated. Like most of the simple and slowly growing tumours, it is enclosed in a fibrous capsule. It is usually multiple.

It is a firm, fleshy, somewhat elastic mass, growing in the muscular wall of the organ. On section the tumour is usually paler, but sometimes brighter in colour than the surrounding muscular tissue. In the smaller rounded tumours the muscular tissue is arranged in concentric laminæ, an arrangement which can easily be discerned with the naked eye; but each lobule of the larger lobulated forms is composed of one of these concentric masses, and between them, running from the capsule, are bands of fibrous tissue, in which blood vessels pass to nourish the new growth. In consequence of this laminated arrangement, the appearance of these masses is frequently compared to that of balls of cotton. In the uterine wall the tumours occur in three positions: (1) Intramural, in the muscular wall itself; (2) submucous, beneath the mucous membrane; and (3) subserous, beneath the peritoneum. The two last push the mucous and serous tissues before them as they grow to the surface and eventually become polypoid.

Harden (§ 62) and stain and mount (§ 438).

($\times 50$).—In the pure myoma the section, instead of presenting a

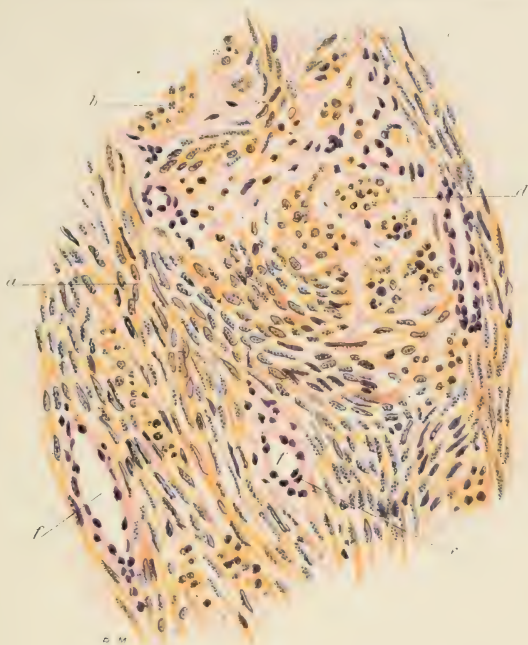


FIG. 226.—Non-striped myoma (uterine fibroid). Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Mass of non-striped muscular tissue, in which the rod-shaped nuclei and the parallel arrangement of the fibrils are seen.
- b.* Similar bundles of fibres cut transversely. The sections of the fibrils have the appearance of rounded cells, the section of the round nucleus is seen as a dot in *some* of the sections.
- c.* Spindle-shaped cells, of which the muscle fibrils are composed.
- d.* Pink fibrous tissue.
- e.* Connective tissue corpuscle.
- f.* Small blood channel.

pink tinge, as in the fibroma (stained with picro carmine or by van Gieson's method), is yellowish-brown with deeply stained nuclear points at intervals. In an old myoma, where there is usually a

considerable quantity of fibrous tissue, the pink fibrous strands stand out prominently between the yellowish-brown muscular bands.

($\times 200$ or 450).—The muscle fibres are identical in appearance with those of ordinary non-striped muscle, but the bundles interlace with one another in every direction. Each bundle is marked by a series of parallel lines; and if the tissue is teased out or if the edge of a section be examined, each fibril marked off by these parallel lines is seen to be composed of spindle-shaped cells, which overlap at their ends to form the fibre. A rod-shaped nucleus may be seen in the centre of each cell. The larger bundles are usually thrown into folds, so that though the lines are parallel, they are somewhat wavy. In certain parts of the section the bundles are cut transversely or obliquely, and in place of parallel lines there are bundles of what appear to be rounded cells, some with, others without, a deeply stained centre. These are simply the muscle cells cut transversely, the section sometimes passing through the rod-shaped nucleus, and sometimes through the contractile part of the cell only.

It is not always an easy matter to distinguish between a true fibroma and a fibro-myoma, and it is therefore well to bear in mind that the fibrous tissue is white, hard, and glistening, whilst the muscular bands may be “pink, reddish-grey, or white,” and are not nearly so firm as is fibrous tissue. To make the diagnosis certain, a microscopic examination should always be made, for which small fragments of the tissue should be prepared (§ 44, 4 and 5). The fibrous tissue then swells up and disappears, and the muscle fibres may be separated and examined, stained or unstained. The rod-shaped nuclei stand out very prominently in such preparations.

Degenerative changes.—(1) Fatty change; (2) mucoid softening; (3) hæmorrhages frequently follow the above conditions, especially where the vessels are numerous; (4) calcification, giving rise to the so-called womb-stone; (5) inflammation in consequence of injury, in which condition the fibres undergo cloudy swelling, and become swollen and granular,—abscess formation frequently following.

NEUROMA

440. It is necessary to mention this tumour, although it is of comparatively rare occurrence. It may assume one of two forms—

(a) composed of nerve fibrils, occurring usually at the cut ends of nerves; or (b) composed of ganglion cells, a case of which is recorded in connection with the suprarenal capsules. Many of the so-called neuromas are in reality fibromas or myxomas on the nerve trunks, or gliomas in the central nervous system.

Prepare as for nerve structures (§ 400).

ANGIOMA

441. The angioma is a tumour made up of dilated blood vessels, some of which appear to be of new formation, whilst others are only dilated pre-existing blood vessels. Along with the dilatation there is frequently an increase in the amount of connective tissue between the vessels.

There are two forms—(1) Cavernous angioma, and (2) simple capillary angioma or teleangioma. The former has already been described (§ 253), and its structure in the skin is very similar, making allowance for the difference in the structure of the tissue or organ in which it occurs.

Prepare as in § 253. Simple or capillary angioma is distinguished from the cavernous form by the fact that although there are fusiform and sacculated dilatations of the new or pre-existing vessels, the general tubular form of the vessels is preserved. In the simple angioma of the skin or naevus (mother's strawberry mark) the dilatation above described is the principal feature; there is little thickening of the walls of the vessels.

Naked-eye appearances.—Such a tumour appears as a bright red or livid patch surrounded by a number of similar small spots which are not raised from the skin. These tumours occur in the position of the closed facial and branchial clefts and near the various orifices of the body; sometimes along lines corresponding to the distribution of a special nerve—the facial branches of the fifth nerve. They are also of comparatively common occurrence in the glioma, and, more rarely, they are met with in the brain, kidney, spleen, uterus, muscles, bones, hollow viscera, and mamma.

(× 50).—Immediately under the epithelium of the skin which is flattened out the papillae have almost disappeared. Note the large number of minute arterial channels cut in transverse, oblique, or longitudinal section. The vessel walls contain a large number of

nuclei, whilst it is evident that they are supported by a delicate



FIG. 227.—Naevus—capillary angioma of the chest wall. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

a. Normal skin.

b. Flattened out rete Malpighii.

c. Angiomatous tissue consisting of very cellular vascular tissue. The blood channels are filled with red blood corpuscles.

d. Normal subcutaneous tissue with hairs, sweat ducts, blood vessels, muscular tissue, etc.

connective tissue matrix in which are numerous cells. This

angiomatous tissue extends from the cutis vera into the muscular tissue beneath, and is sharply separated from the surrounding tissues, though here and there small bundles of fibrous tissue may be seen projecting into the vascular or capillary mass.

($\times 300$).—The structure of the small vessels with their well-defined endothelial lines can easily be made out. Where the vessels are very small the tissue is markedly cellular, many of the cells being apparently of endothelial origin, though plasma cells and



FIG. 228.—Nævus—capillary angioma of chest wall. Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Highly cellular embryonic vascular tissue.
- b.* Vascular channels, lined with endothelial cells, and containing blood. Note the lymph spaces around these vessels.

lymphocytes may also be seen in considerable numbers. Around some of the vessels are well-defined lymph spaces lined with endothelial cells, and around these again are connective tissue fibrils on or in which are lying a number of fibroblasts. The vessels vary very greatly in size.

In another form of simple angioma the dilatation is not so great, but the increase of tissue around the vessels is more marked, as in hæmorrhoids, which are found in the submucous tissue of the rectum,

and consist of masses of small dilated veins with thickened walls, supported by an increased quantity of connective tissue.

Harden (§ 62), cut (§§ 91–96), stain (§ 103), and mount (§ 199).

On microscopic examination the principal points to note are the dilated saccules, connected by the vascular tubes; the well-marked endothelial lining of the blood-distended cavities; and in some cases the thickening of the vascular walls, the result chiefly of an increase in the thickness of the adventitia.

A similar condition of the lymphatic vessels and tissues occurring in the tongue, lips, and extremities, specially in the inguinal region, is described under the term lymphatic angioma, or lymphangioma. It is found near the orifices or embryonic clefts—small tumours composed of groups of more or less transparent vesicles, composed of an irregular mass of newly formed dilated lymph vessels. It is a reticulated mass of tissue lined with endothelium, with fatty, connective, or myxomatous tissue between. The spaces filled with lymph communicate with the lymphatic vessels.

LYMPHOMA

442. The true lymphoma is a histioid tumour; but along with it must be described two other forms of lymphoid growth,—the lymphadenoma and lympho-sarcoma,—both of which depart somewhat from the true histioid type, and, unlike the true lymphoma, are often very malignant.

The lymphoma appears in many cases to be rather a hyperplasia of lymphoid tissue than a true tumour, and it is always found in positions in which lymphoid tissue is normally present, as in lymphatic glands in the intestine, uterus, kidney, etc.; but occasionally there are true lymphoid tumour growths.

Naked-eye appearances.—It occurs as a solitary mass, does not attain any great size, and is usually surrounded by a more or less dense fibrous capsule. On section it is uniformly soft, and white or pale pink in colour. Where small hæmorrhages have occurred, it may have yellow or brownish points (altered blood pigment). From this circumstance, and from the general appearance of the growth, it may in some cases be mistaken for a sarcoma, but the history and histological structure, together, will at once set any doubts at rest.

Harden (§ 60 or 62) and stain (§§ 102–104 or 110 (*b*) and 132).

($\times 50$).—Note that the structure is essentially that of normal

lymphoid tissue. The deeply stained nuclei of the cells are seen in great numbers; here and there running through the mass are capillary vessels. If one of these vessels near the edge of the section be examined, delicate bands of pink tissue may be seen attached to its walls; and in favourable specimens, where the rounded cells have been displaced, a delicate reticulum may be distinguished. Lying on the junctions of the strands or fibrillæ of the network, and clasping them with their processes, are large nucleated branching endothelioid or connective tissue cells. A number of larger vessels are also present, with similar fibrils attached to their walls. To distinguish more clearly the elements of which the tissue is composed, shake a thin section of the tumour in a test-tube containing a small quantity of $\frac{3}{4}$ per cent. salt solution (§ 36. 5); spread out carefully on a slide and stain (§ 132). The stroma attached to the capillary walls can then be readily distinguished. It is said that in the lymphoma the capillaries are distended, but it is extremely difficult to make this out.

($\times 300$).—The attachment of the stroma to the capillary walls is more easily seen. At the junctions of the bands of the stroma are large branching endothelioid cells with branching processes which clasp the bands of the stroma and extend along them for some distance, but are quite distinct from them; each has one or two nuclei which stain deeply and so stand out prominently. Ranvier holds that these endothelioid cells are the cells by which the fibrillæ are secreted or formed. This is a fact to be borne in mind when considering the other forms of lymphoid tumours. Lying in the meshes of the network are small round lymphoid cells, which are stained almost throughout, showing that they are composed of a nucleus surrounded by an extremely thin film of protoplasm. Some of the cells are larger, and may contain a couple of nuclei, and in a few instances, especially where there have been small hæmorrhages, they may contain granules of brown pigment. Where the capillaries have ruptured, the blood may be seen as greenish corpuscles, lying in the meshes around them.

LYMPHO-SARCOMA

443. The second form of lymphoma—the lympho-sarcoma—is a malignant growth, which, from its clinical history and pathological

appearances, is frequently mistaken for sarcoma or encephaloid cancer. It may grow in any position, but usually begins in the lymphatic glands or tissue of the viscera, from which it spreads, especially to the lungs; it may grow to a considerable size, and is often multiple. The so-called primary cancer of the kidney is often a lympho-sarcoma. The section from which the following description is taken was removed from one of the mesenteric glands.

Naked-eye appearances.—The growth resembles an ordinary lymphoma; but is more pink, slightly more vascular, and of a somewhat softer consistence throughout. Around the soft, almost diffuent, mass is a delicate fibrous capsule. On section are seen numerous yellow or brown spots, due to rupture of the vessels and the presence of extravasations of blood of different ages. On scraping the surface a quantity of creamy fluid is removed. Examine this in neutral saline solution (§ 36. 5) $\times 300$, and note that it is composed chiefly of lymphoid cells, similar to those described as occurring in lymphoma. Prepare as in § 442

($\times 50$). — In the hardened section the lymphoid cells predominate to such an extent that no other structures, except a few blood vessels, and around them at intervals the green hæmorrhagic masses, can be distinguished, either under the low or high power; the tumour resembles, very closely, the small round-celled sarcoma (§ 453).

Now examine a pencilled or shaken section. A few of the small blood vessels may be seen, and at certain points, where the lymphoid cells are washed away, an exceedingly delicate reticulum can be distinguished. This reticulum is similar to that present in lymphoma, but is much more delicate; the meshes are larger, and the endothelioid plates are neither so prominent nor so numerous. In the small round or ovoid cells the nuclei, and therefore the cells, appear to be undergoing more rapid division than in lymphoma.

($\times 300$).—The increased proportion of small round cells to reticulum, and the relatively small number of endothelioid plates on the network, can now be better appreciated. Note the small collections of coloured blood corpuscles, the result of hæmorrhage from the “embryonic” and badly supported vessels. The delicate stroma at once enables the observer to distinguish this growth from the small round-celled sarcoma, which, otherwise, it resembles so closely.

LYMPHADENOMA (HODGKIN'S DISEASE)

444. In Hodgkin's disease, as already seen (Liver, § 248 ; Spleen, § 351), there is an overgrowth of certain elements of the lymphoid tissue. The first manifestation of the disease is a growth in the lymphatic glands, usually of the neck or groin. From the primary centre, the surrounding glands and then the spleen, liver, kidneys, lung, submucous tissue of the intestine, serous membranes, skin, heart, and suprarenal capsules are all, in turn, involved in a malignant infective process.

Naked-eye appearances.—The lymphadenomatous tissue in the lymphatic glands is firmer than, and not so liable to caseate as, that in the viscera, otherwise the growths are identical in both naked-eye and microscopic appearances. It occurs either as small firm elastic masses, or as large pinkish-white nodules, though in the liver, spleen, and kidneys, especially where there is a tendency to caseation, there is a yellower tinge from the beginning, and the tumour is doughy and even putty-like. Hæmorrhages, such as those met with in lymphoma and sarcoma, are comparatively rare.

There is here, as described in the spleen (§ 352), an enormous increase in the number and activity of the endothelioid plates, and a corresponding increase in the amount of fibrous stroma or reticulum, which, however, seems to compress the lymphoid cells out of existence ; in consequence of this their number is diminished.

Harden a section of lymphadenoma taken from any of the lymphatic glands (§ 62), stain (§§ 102–104), and mount (§ 195 or 199).

($\times 50$ and $\times 300$).—In the growing part of the tumour there is a great increase in the number and activity of the endothelioid cells, followed by an increase of the bands of the reticulum, both in thickness and in number, so that there is a gradual conversion of the reticulum into a mass of fibrous tissue, the lymphoid cells becoming more and more sparse as the fibrous tissue is more fully formed. As in the spleen, the lymphadenomatous tissue gradually invades and destroys the surrounding tissue.

Lymphoma—ordinary lymphoid tissue ; endothelioid plates and reticulum both well developed ; number of lymphoid cells normal.

Lympho-sarcoma—small number of endothelioid plates ; correspondingly scanty reticulum ; enormous increase in the number of lymphoid cells.

Lymphadenoma—early increase in the number and activity of the endothelioid plates, accompanied by an increase in the reticular tissue which leads to great diminution of the lymphoid cells.

From the above statement it will be seen that, as in connective tissue, the quantity of the reticulum varies directly as the number of endothelioid plates, but inversely as the number of lymphoid cells.

COMPOUND HISTIOID TUMOURS OR HISTIOID TUMOURS COMPOSED OF MORE THAN ONE TISSUE

PAPILLOMA

445. The papilloma—under which heading are classed warts, horns, the compound cauliflower excrescences, and such polypoid growths as occur in the bladder and in the larynx—consists essentially of a hypertrophied and often branched connective tissue papilla, covered with a hypertrophied layer of epithelium. Examples are the ordinary wart, the large cauliflower excrescences which are so frequently met with round the anal or genito-urinary orifices in syphilitic and gonorrhœal patients, the horns seen on the face and neck, and villous papilloma of the bladder. Although these tumours may grow rapidly, they are non-malignant, and are of purely local origin.

Harden small pieces of one of the compound cauliflower excrescences (§§ 62, 60, and 71), stain (§§ 102–104 or 110 (*b*) and 132), and mount (§ 195 or 199).

($\times 50$).—The general outline of the growth must first be noticed. In place of the simple papilla there is a branching mass of fibrous or fibro-cellular tissue. In this the cells may be numerous if the tumour is of very rapid growth. Supported in this fibrous or fibro-cellular basis are numerous blood vessels, very similar to those in a normal papilla, except that they are usually somewhat larger. At the point of junction with the subjacent tissues these vessels appear to open into large vascular sinuses or dilatations. In consequence of the branching of the connective tissue basis, masses of it may be seen in transverse section, apparently embedded in the epithelium. Lying immediately on the connective tissue is a layer of somewhat columnar epithelial or epidermic cells, which take on any nuclear stain very readily; this corresponds to the germinal layer of the rete Malpighii or rete mucosum. Above this is a thicker layer, in which the cells do not take on the

nuclear stain so readily and are seen to have more formed material, and to be polygonal in shape, corresponding to those in the upper part of the rete Malpighii. Passing farther outwards, a second deeply stained layer is reached—the stratum granulosum of Langerhans. Above this the stratum lucidum is not very distinctly seen under this

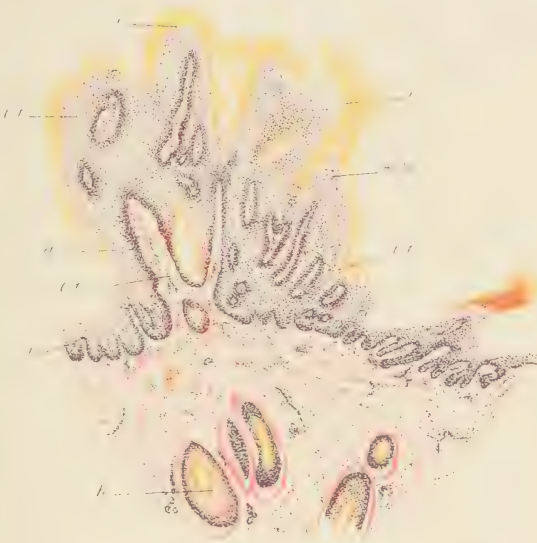


FIG. 229.—Section of papilloma. Wart of scalp. Stained with alum hematein and picro-erythrosin. ($\times 50$.)

- c.* Horny layer.
- R.M.* Rete Malpighii.
- C.t.* Connective tissue basis.
- g.* Germinal layer of epithelium.
- h.* Section of hair and sheath.
- i.* Normal cutaneous epithelium.

power, and the stratum corneum is represented only by an exceedingly thin streak, which does not take on nuclear stains at all, but is stained by picric acid and similar stains.

($\times 300$).—Examine the blood vessels distended with blood and the fibro-cellular stroma, in the young cells of which the nuclei can fre-

quently be seen undergoing division. Then note the layer of columnar epithelial cells, with their deeply stained nuclei. Above this layer the cells are first irregularly round and then polygonal, and many of them have well-marked "prickles" passing into the body of the cell, these

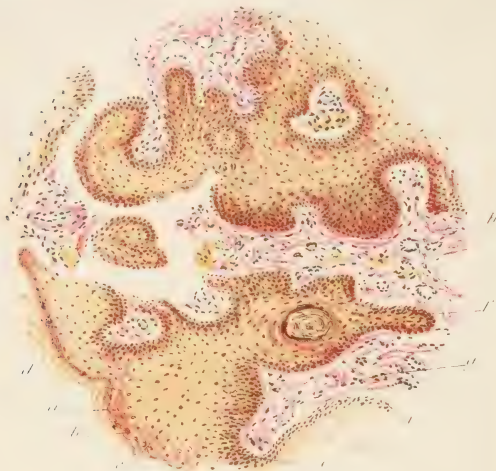


FIG. 230.—Section of a papilloma of the cheek. Stained with alum hæmatein and picro-erythrosin. ($\times 90$.)

- a.* Horny squames on surface of growth.
- b.* Layer of flattened cells from near the surface of the rete Malpighii.
- c.* Well-formed prickle cells.
- d.* Vacuolated prickle cell.
- e.* Smaller rounded or polygonal cells, immediately above.
- f.* The columnar or germinal layer.
- g.* Cellular connective tissue of papillary basis.
- h.* Blood vessels.
- i.* Concentric colloid layers, squamous epithelial cells forming cell nests almost like those met with in the squamous-celled epithelioma.

often appearing to be directly continuous with processes from the nucleus, though in some cases the nucleus is surrounded by a distinct vacuole. The processes of adjacent cells are continuous with one another, and may be seen to pass from nucleus to nucleus in all directions. The stratum granulosum is very well developed; its cells

are granular and deeply stained at the poles, but in the body of the cell there is a clear bright space. Each cell is more or less spindle shaped. The stratum lucidum may be distinguished under a high power, but it is never very well developed in the true papilloma, and the stratum corneum, too, is represented in a picro-carminic or van Gieson stained section merely by a thin bright yellow band of horny squames. Here, then, the distinguishing features are the enlargement

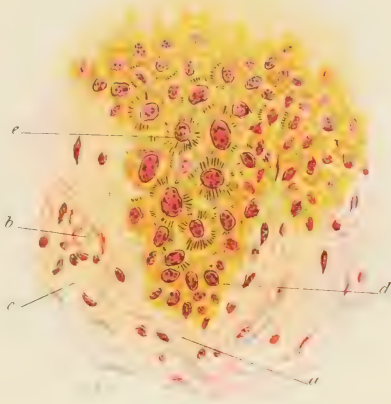


FIG. 231.—Drawing of epithelium from a rapidly growing papilloma.
Stained with picro-carminic. ($\times 450$.)

- a. Fibrous tissue of true corium.
- b. Small blood vessel.
- c. Lymph spaces.
- d. Cells of germinal layer.
- e. Well-formed prickle cells in the rete Malpighii.

and branching of the papillae, the enormous development of the rete Malpighii and stratum granulosum, and the thinness of the horny layer.

446. Papillomas of the mucous membrane grow in the same way, but are covered by epithelium, similar to that which is normally present in the position from which they grow. The soft velvety growths which are met with in such positions as the bladder and intestine belong to

this group. In the bladder they are seen as small soft vascular tumours which bleed very readily and from which thread-like processes project, giving the growths a peculiar villous appearance. They may be single or multiple, and are usually situated at the base of the bladder in the



FIG. 232.—Section of a villous papilloma of the bladder. Stained with alum hæmatein and eosin. ($\times 50$.)

- a.* Delicate connective tissue stroma or core in which may be seen
- b.* Blood vessels and
- c.* A few connective tissue corpuscles.
- d.* Columnar epithelium arranged in several layers.
- e.* Transverse section of a small process of this growth in which a central connective tissue core and surrounding columnar epithelium are well seen.

trigone, and especially around the orifices of the ureters. They are often found associated with inflammation of the mucous membrane of the bladder. The tissue is so delicate that small portions are readily detached. On floating the tumour tissue out in water this delicacy of

the threads may easily be made out. Usually they do not go deeper than the mucous membrane, but in rare cases they appear to assume a malignant character.



FIG. 233.—Section of villous papilloma of the bladder. Stained with alum hæmatein and eosin. ($\times 200$.)

- a.* Delicate connective tissue stroma, with
- b.* Branching cells.
- c.* Hyaline cells.
- d.* Polymorpho-nuclear leucocytes.
- e.* Blood vessel lined with flattened endothelial cells.
- f.* Fibroblasts.
- g.* Several layers of columnar cells with large nuclei and distinct nucleoli.

Harden (§ 61, 63, or 64), cut (§ 82 or 94), stain (§§ 102–104 or 110 (*b*)), and mount (§ 195 or 199).

($\times 50$).—The stroma is exceedingly delicate. It contains numerous blood vessels, which appear to be somewhat imperfectly supported by an open cellular connective tissue. The branching processes of

these villous growths are covered with layers of epithelium very similar in appearance to those met with in the bladder, but usually somewhat more distinctly columnar. On transverse section of these processes the central "core" is seen to be small, whilst the epithelium occupies a comparatively large proportion of the section.

($\times 300$).—The delicate connective tissue stroma with a number of polymorpho-nuclear leucocytes and hyaline cells, the imperfectly supported blood vessels, and the stratified layers of epithelium, are very evident.

HORN Y PAPI LLOMA

447. If a section be made of a "horn" taken from the face or the neck, and stained as for papilloma, the stratum corneum is seen as a dense yellow mass, which appears to fill up every crevice on the outer surface of the growth; it forms a layer of very considerable thickness over the stratum granulosum, which therefore does not stand out quite so prominently as in the ordinary papilloma. In order to understand this appearance the situation of these growths must be remembered—face, neck, and those surfaces generally on which there is secretion of a large quantity of sebaceous material. The horny layer, instead of being constantly shed, as from a normal cutaneous surface, or from the surface of an ordinary papilloma, is glued together by a large quantity of sebaceous material, and a kind of pasty concrete is formed, which, drying and hardening, constitutes the smooth horny mass. All the other features described as present in the ordinary papilloma are here repeated.

SIMPLE ADENOMA

448. A simple adenoma of the breast or of the thyroid gland may be taken as the typical adenoma. It is a mass of glandular tissue growing from a separate centre of acini and tubules apparently unconnected with those of the mammary or thyroid gland. In the true adenoma there is more than a mere increase in the amount of interglandular tissue. There is actual gland formation, accompanied in many cases by a growth of inter-acinous connective tissue, and also by a distension into cysts of the newly formed acini and tubules. Pathologists differ greatly as to the definition and even as to the nature of adenoma, and cystic sarcomas and primary cancers have been classed under this heading, but it will be well to distinguish the adenoma from

the cancer in the same way as the papilloma is distinguished from the epithelioma, though in both cases, under certain conditions, the one may be succeeded or replaced by the other.

Naked-eye appearances.—The adenoma is a rounded or lobulated



FIG. 234. —Simple adenoma of the breast. Stained with alum hematein and eosin. ($\times 50$.)

- a. Distended acini or spaces lined with cubical epithelium and extending into a mass of new fibrous tissue.
- b. Cellular connective tissue cells proliferating around more rapidly extending acini.
- c. Small ducts lined with cubical epithelium.
- d. Blood vessels in connective tissue.

tumour, varying greatly in size, from that of a filbert to that of a child's head, usually surrounded by a fibrous capsule, by which it is sharply defined from the neighbouring tissue. It grows slowly; there is no central umbilication, and no retraction of the nipple, such as is met with in scirrhus cancer, for which only the adenoma is liable to be

mistaken. There are no secondary growths in the neighbourhood, and there is no implication of the glands.

On section such a tumour appears to be composed of a mass of fibrous tissue, over which are scattered small chrome yellow or cream-coloured points (the masses of epithelium), and cysts of various shapes and sizes in large numbers, from which a quantity of creamy, opaque, serous, gelatinous, or semi-solid material may be

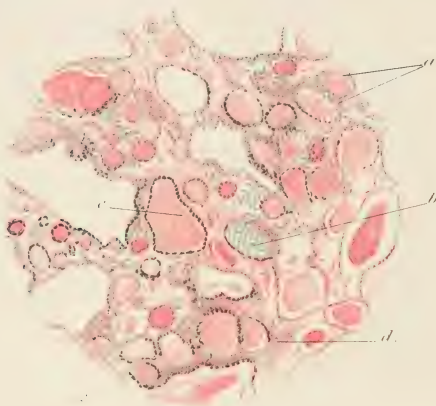


FIG. 235.—Cystic adenoma of the thyroid gland. Stained with alum haematein and van Gieson's stain. ($\times 90$.)

- a.* Single or double row of epithelial cells, of which the nuclei only are seen.
- b.* A more irregular mass or cylinder of epithelial cells.
- c.* Cyst filled with colloid material.
- d.* Delicate connective tissue basis.

expressed. In some cases the adenoma consists of a soft, pinkish mass, through which run vascular bands, surrounded by a fibrous capsule.

Harden (§§ 60 and 62 or 64) and stain (§§ 102 or 104 and 110 (*b*)).

($\times 50$).—A regularly formed fibrous matrix, more or less cellular, according to the rapidity of the growth of the tumour, is seen. Running through this are numerous blood vessels, and supported by it are tubes or acini in various stages of development, seen as solid

columns of cubical epithelial cells, perfectly formed tubes with distinct lumina, or cysts of considerable size; at certain points may be observed the process of the opening out of the lumen from the solid mass of cells to the distinct cavity, lined with a layer of regularly arranged cylindrical or cubical cells.

($\times 300$).—Examine the fibrous stroma in which the blood vessels are embedded. Lying immediately on it, and apparently taking the place of the basement membrane of the normal gland tissue, is a layer of delicate flattened cells—Debove's layer. Above this layer is, usually, a single layer of non-ciliated columnar or cubical cells, each with a distinct and well-formed nucleus. A somewhat deceptive appearance is frequently presented, especially when the sections are not very thin; in some of the cavities it appears as though there were several rows of cells, because the knife, passing obliquely through the same layer of cells, exposes a somewhat elongated surface view, hence the appearance of several layers. Again, if the section be made through the epithelial lining at the margin of the cyst, an apparently solid mass of epithelium is presented to our view. It is very necessary to remember this in making an examination of adenomas.

The adenoma is developed in much the same way as is the mammary gland (probably from a portion cut off from the main mass of this gland), for a description of which the student is referred to works on embryology and histology.

MULTIPLE, COMPOUND, OVARIAN CYSTIC TUMOUR

449. Synonyms, "Proliferous Ovarian Cystic Tumour"; "Multifollicular Ovarian Tumour."

The ovarian cystic tumour is a growth which, in its mode of development, non-malignant character, and general structure, may be compared to the adenoma, and may be termed the adenoma of the ovary or of the peritoneum.

It may reach an enormous size, and is usually composed of a series of cysts, situated either in the ovary or in the broad ligament. The tumour is surrounded by a fibrous capsule, and on section the cavities are found to be bounded either by dense fibrous bands or by spongy tissue, which, examined with a magnifying lens, is seen to be made up of a number of small cysts, in which are minute glistening or gela-

tinous specks. The larger cysts usually contain a quantity of watery or serous fluid, in some cases almost like the fluid found in a hydatid cyst, with chloride of sodium, and but little albumin. This fluid may be variously coloured by altered blood pigment—purple, red, or yellow. The smaller cysts are filled with a gelatinous material, which is rarely blood stained, but contains more albumin.

Harden a small piece of the spongy part of the tumour, in which minute glistening or gelatinous specks are to be seen (§ 59 or 64), stain (§§ 102, 103, or 110 (*b*), and 132), and mount (§§ 195 and 199).

($\times 50$).—Embedded in a somewhat cellular and highly vascular connective tissue stroma are numerous small cysts. The nuclei of the connective tissue cells are deeply stained with carmine or hæmatein, and stand out prominently. The blood vessels are filled with blood corpuscles. The cysts are very irregular in outline; some are round or oval and simple; others are subdivided by papilliform processes which run from the connective tissue stroma, and in some cases meet in the centre and divide the primary cysts into smaller compartments.

Lining each cyst is a regular layer of epithelium, columnar and often ciliated, or excavated to form goblet or chalice cells. The nuclei of these cells can be distinctly seen, and are usually situated in the lower third, especially of the chalice cell. Notice that all the papilliform projections are completely invested with this regular layer of epithelium.

($\times 300$).—Examine the cellular stroma, with its numerous blood vessels, and then the arrangement and appearance of the epithelial cells. There is no proper or distinct basement membrane, and in this feature the tumour resembles the malignant adenoma; but, as in the adenoma of the breast, a layer of flattened nucleated cells is found between the columnar cells and the connective tissue—Debove's layer. From these flattened cells spring the larger cells, which are arranged in a single or a double row. The deeper cells are more cubical than columnar, and interlock with those of the more superficial layer. The superficial cells are tall and columnar, a few of them are ciliated, but the greater number are chalice cells, in which the nucleus is placed in the lower third. The nucleus is deeply stained, and stands out very prominently from the more delicately stained cell. In the chalice cell the part above the nucleus bulges out slightly before the mouth of

the cell is reached, which may be seen as an ovoid opening. The bulging part is more transparent than the lower third of the cell.



FIG. 236.—Drawing of section of a compound ovarian cystic tumour.
Stained with picro-carmin. ($\times 300$.)

- a.* Fibro-cellular connective tissue stroma.
- b.* Layer of flattened cells, or Debove's layer.
- c.* Single layer of chalice cells.
- d.* Several rows of cells, of which the nuclei are seen.
- e.* Mouths of the chalice cells.
- f.* Mucoid material contained within the cyst.

Within the cyst a few cells are usually lying free, embedded in a delicately tinted mucoid or colloid material.

CYSTS

450. Cysts have already been described as present in the liver (§ 252) and kidney (§ 285), where they result from dilatation of obstructed ducts, the accumulation of various epithelial or fluid materials, and the distension of pre-existing spaces.

Other cysts have been described in the liver as due to the presence of parasites (hydatid cysts) or foreign bodies, cystic new formations.

Others, again, spurious cysts, are formed by softening and degeneration in new growths, as in the case of the cystic myxoma (false cysts, or cysts of degeneration).

Cysts of new growth are also met with, as in the adenoma and the compound ovarian cystic tumour.

Peritoneal cysts are found as hydrocele and loculated cysts, in which the peritoneum is prolonged into a small cavity or series of cavities, separated from the main sac, which are then distended to form a cyst or cysts; secondary cysts are budded off, as it were, from the primary sac, and they in turn are distended.

Ranula.—This term is applied to the cysts which are found under or near the tongue, as the result of dilatation of the ducts of the sublingual submaxillary and retro-maxillary glands. It includes those large cysts, distended mucous glands and ducts of Blaudin-Nuhn which lie beside the frenum linguæ, extending forward to the frenum, lined with ciliated epithelium, and filled with thick, somewhat tenacious, fluid containing mucin, chloride of sodium, albumin, and a few epithelial cells; these are the result of dilatation of the ducts of the glands, and not of any part of the gland itself which continues to secrete the material with which the cysts are distended. Other forms of ranula are described, but they are comparatively unimportant.

Endothelial cysts, such as bursæ, occur round tendons, and are caused by distension of their sheaths by exudation.

Distension of closed cavities may give rise to cyst formation, retention cysts, as in hydro-nephrosis and ranula; or exudation cysts, as in the case of goitre, where large cysts are formed by distension of the normal closed sacs of the thyroid gland; by a proliferation of the epithelium lining the cavity, followed by colloid degeneration of the cells, as in the case of the colloid cysts derived from the renal epithelium (§ 285).

Developmental cysts are also met with (*a*) where there is imperfect closure of foetal ducts or canals, and (*b*) where we have adhesion or occlusion of an imperfectly developed embryo.

DERMOID CYSTS

451. The "Dermoid" cystic tumour deserves more than passing mention. It is usually found in or near the ovary in the peritoneum,

when it is often large and complicated; smaller and simpler forms are found near the sacrum and at the side of the neck and face.

Naked-eye appearances.—The tumour from which the following description is taken was removed from the ovary, and was about the size of a child's head at birth. It was firm at points, but from the surface a number of cysts projected. Some of these contained a quantity of glue-like fluid, others a soft, fatty, or sebaceous-looking material, whilst others again were filled with long hairs disposed in coils. When the mass was cut into, the knife "creaked" through nodules of cartilage, and then "grated" through calcareous or calcified patches. In the body of the tumour were larger cysts, though some parts of the growth were simply fleshy. Portions of the mass were hardened (§ 64), and treated as for adenoma (§ 448). On microscopic examination this dermoid cyst appeared to be an attempt at the formation of a fetus within the ovary itself, as almost every tissue present in the human body could be distinguished—epithelium, squamous, evidently on a cutaneous surface; goblet cells, as from the intestine; ciliated, as from the trachea; hair follicles, with the deeply-stained yellow hair in the centre, in transverse and longitudinal section; cartilage, with well-developed capsules and matrix; muscle fibre, both non-striped and striped; blood vessels in all stages of development; gland structures similar to those found in the bronchi, in the skin, and in the duodenum; small fragments of bone in process of calcification—in some parts the matrix is stained like fibrous tissue, in others like a calcified matrix; nerve fibres; multipolar nerve cells similar to those met with in the anterior horn of the cord; ganglion cells or large rounded cells with well-marked nuclei and long processes, such as are normally met with in the semilunar ganglia; masses of lymphoid tissue; fat globules; fibrous tissue, and tendon. The large cysts were all lined with ciliated or goblet-celled epithelium, except those into which hairs were growing, where most of the cells were more like ordinary cutaneous epithelium.

SARCOMAS

452. The sarcoma, as already defined, is a tumour composed of mesoblastic tissue in an *imperfect state of development*; owing to the fact that there *is always an attempt* at the formation of some of the higher tissues, there are many varieties of sarcoma. The tumour

may be simply a mass of granulation tissue, or there may be in it a *partial* formation of fibrous tissue, cartilage, bone, striped muscle fibre, etc.; with a corresponding modification of both the naked-eye and the microscopic appearances of the growth.

SMALL ROUND-CELLED SARCOMA

453. This, the simplest form of sarcoma, is composed of the most elementary type of connective tissue, typical embryonic or granulation tissue, and is perhaps the most malignant of the group. It grows very rapidly, infiltrates locally, and, spreading by the blood vessels, may give rise to numerous secondary growths.

It occurs especially in the fasciæ and in the loose areolar and subcutaneous tissues, in the connective tissue of the nerve centres, retina, bones, muscles, testicle, and mamma, as a primary growth; but it does *not* affect the lymphatic structures. As a secondary growth it almost invariably makes its appearance first in the lungs, after which it affects the more vascular organs, especially those in which there is a complex capillary system.

Naked-eye appearances.—This form of sarcoma is very soft, in some cases almost pulpy, or is like a piece of brain tissue; it is usually rounded, and, to the naked eye, sharply defined from the surrounding healthy tissue, but has no fibrous capsule. On section it is pale pink, has no distinct glistening white fibrous streaks, though firmer bands are found running through its substance, but yellowish or creamy patches—due to fatty degenerative changes—are frequently observed on the surface. Still more characteristic are the small red, brown, and yellow points—hæmorrhagic patches in various stages of alteration. Hæmorrhages are common in all forms of sarcoma, but especially in this and in the myeloid form (§ 457).

Harden (§ 62, 63, or 64), stain (§§ 102, 104, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—Observe the mass of small round cells gradually invading or infiltrating the surrounding tissues; in a sarcoma growing in muscle, the fibres are gradually separated by the infiltrating small round cells. Where the tumour tissue is very distinct, a series of lines of elongated cells may be distinguished, usually arranged in double rows, between which coloured blood corpuscles may be seen. These double rows of cells are the embryonic blood vessels. The

great resemblance of this mass to granulation tissue will be recognised at once (§§ 222–225).

($\times 300$, or better, $\times 450$).—The elementary cell structure is now

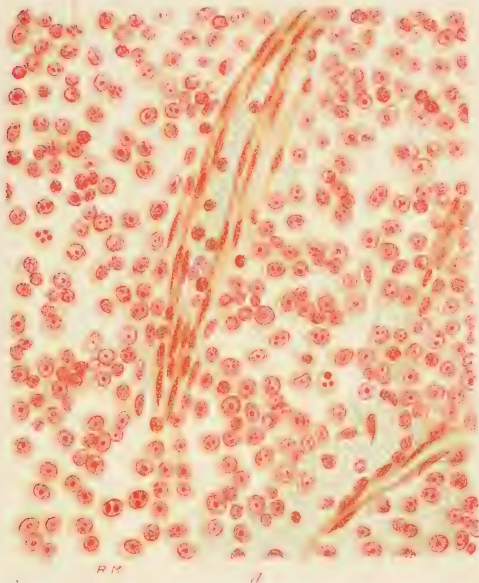


FIG. 237.—Small round-celled sarcoma. Stained with picro-carmin.
($\times 400$.)

- a.* Small round cells with large nuclei and distinct nucleoli.
- b.* Flattened spindle-shaped cells, forming the walls of embryonic blood vessels.
- c.* Flattened cells between ordinary tumour cells and spindle cells of the vessel wall. Row of red blood corpuscles between.
- d.* Haemorrhage.

In some of the cells we have distinct evidence of rapid proliferation. Double nucleoli and elongating and constricted nuclei.

easily distinguished. The majority of the cells are from $\frac{1}{2500}$ to $\frac{1}{1000}$ inch in diameter (all larger than a coloured blood corpuscle, which is about $\frac{1}{3200}$ inch). There is no cell wall, but each cell has

a distinct deeply-stained nucleus, $\frac{1}{5000}$ to $\frac{1}{2500}$ inch in diameter, within which nucleoli are to be observed as deep crimson dots. Between the cells is a very small quantity of granular homogeneous intercellular substance, which, however, in many cases, may be almost indistinguishable. The elongated cells seen above are only sarcoma cells, and have taken their present shape because of the pressure to which they have been subjected by the blood corpuscles, which appear to have simply been forced in between them. The blood vessels in this growth are quite embryonic in type; their walls, composed of these modified sarcoma cells, are exceedingly delicate, and the least extra strain causes them to give way, when blood is poured out into the surrounding sarcomatous tissue. Examine a transverse section of a vessel, and note the flattened layer of cells next to the blood current, and the gradual transition in the successive layers from the flattened to the rounded cell, so that the tumour cells are in direct contact with the blood current, by which they are carried to the lungs—where secondary growths first make their appearance—and then to the other vascular organs.

The degenerations to which this variety is liable will be best considered with those of the other sarcomas.

LARGE ROUND-CELLED OR MIXED SARCOMA

454. The large round-celled sarcoma grows in much the same positions as the above, but affects specially the submucous tissue of the pharynx and posterior nares, where it forms a small, firm, almost fibrous, pale polypoid mass, sharply defined from the surrounding healthy tissues. It is malignant in a much lower degree than the small round-celled sarcoma, and rarely gives rise to secondary growths.

Harden (§§ 59–64), stain (§§ 102–104, 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$) and ($\times 300$).—Note that the rounded cells are about two or three times as large as the cells of the small round-celled form. Each contains from one to four large ovoid nuclei, surrounded by a quantity of protoplasm. Between them is a delicate fibrillated intercellular substance, which at certain points is collected into thicker bands. These, along with thin-walled vessels, divide the large cells into groups, which vary considerably in size. At other

points, especially where the fibrillar tissue is present in large quantity, elongated or spindle cells may be seen, almost like those in organising

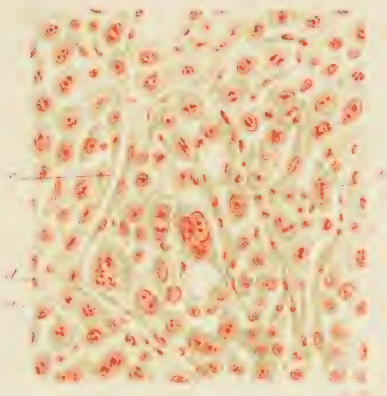


FIG. 238.—Section of mixed large-celled sarcoma, stained with picrocarmine. ($\times 300$.)

- a.* Large irregular cell with three nuclei.
- b.* Spindle-shaped cell with nucleus dividing.
- c.* Smaller round cell with single nucleus.
- d.* Delicate intercellular substance.
- e.* Embryonic blood vessel, bounded by smaller flattened or spindle cells.

granulation tissue. The vessels, as in all sarcomas, are quite embryonic in type, having thin cellular walls.

SPINDLE-CELLED SARCOMA

455. In the spindle-celled sarcoma there is an attempt at the formation of more highly organised connective tissue than occurs in the small round-celled form. The cells become elongated, in most cases the amount of intercellular substance is increased, and the development of the vessels is carried somewhat further.

Of these tumours the more important are the following :—

RECURRENT FIBROID TUMOUR

The recurrent fibroid of Paget, like the other tumours of this group, may grow from almost any connective tissue, but especially in fasciæ, periosteum, the breast, kidney, liver, skin, and dura mater. In the cases recorded by Paget they appear to grow principally from the periosteum and subcutaneous tissue in various parts of the body. They vary in size from half an inch to as much as a foot in one of their dimensions, and are characterised by their tendency to recur locally when imperfectly removed ; they have no special tendency to infiltrate.

Naked-eye appearances.—In the first instance they do not give rise to secondary growths, but when they have been repeatedly removed the recurrent mass very frequently comes to resemble the true spindle-celled sarcoma (§ 456). They are rounded or lobulated, and are firmly attached to the tissue from which they grow. On section this tumour is firm, tough, and irregular, and often has a fleshy look. It may be pale pink or brownish red, almost like a fibroma, and the surface has a streaky look. It is from this appearance that the name “fasciculated sarcoma” is derived.

Harden (§§ 59–64), stain (§§ 102–104, 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—Note the fasciculated appearance. A series of bundles of cells may be seen interlacing with one another in all directions ; some of these are cut longitudinally, others obliquely, others again transversely. The blood vessels are fewer but are slightly more highly organised than are those in the small round-celled sarcoma.

($\times 400$).—The bundles are seen to be made up of “narrow, spindle-shaped, elongated, caudate, and oat-shaped nucleated cells.” The nucleus is said to distend the body of the cell at the point at which it is present. Some of the cells have bifurcated ends, but the majority of them are oat-shaped, and between them is a small quantity of fibrillated intercellular substance.

TRUE SMALL SPINDLE-CELLED SARCOMA

456. This tumour grows in much the same positions as the foregoing, and, though rather more malignant than the above, it does not

often give rise to secondary growths. When these do occur, they are found in the same position (the lung first, and then other vascular organs) as the other secondary sarcomatous growths.

Naked-eye appearances.—It may attain a considerable size, is surrounded by a more or less definite capsule, and on section presents



FIG. 239.—Small spindle-celled sarcoma. Stained with alum hæmatein and van Gieson's stain. ($\times 200$.)

- a.* Well-formed spindle cells.
- b, b'.* More elongated spindles bounding vascular channels.
- c.* Cells cut transversely appear to be small round cells.
- d.* Larger cells in which there is indirect division of the nuclei.

a firm, solid, or elastic, pale, fleshy surface—not so smooth as in the recurrent fibroid form—and with the glistening or fibroid streaks more pronounced. Prepare as above, and examine.

($\times 50$) and ($\times 400$).—The spindle cells are more perfectly formed, and, as a rule, are somewhat larger and more elongated than are those

of the recurrent fibroid tumour. They are arranged in bundles, which interlace in all directions, so that they are seen in various sections. Those cut longitudinally are the ordinary spindle cells, with ovoid, or, in some cases, rod-shaped nuclei. Others are cut obliquely, and these appear to be ovoid cells; whilst others again, cut transversely, appear to be round cells. It must be noticed, however, that these sections are comparatively small, and that some of them have no nucleus, owing to the fact that the sections are made near the ends of the cells to which the ovoid nuclei do not extend.

Where the section passes transversely through the centre of a cell the nucleus, of course, is divided, and the rounded section appears to have a nucleus.

Running through the section are embryonic blood vessels similar in structure to those met with in the small round-celled sarcoma, but not so numerous. There is little intercellular substance.

MYELOID SARCOMA

457. The myeloid or giant-celled sarcoma, the most common variety of the small spindle-celled sarcoma, is one in which are well-formed giant cells, these being present probably because of the positions in which the tumour occurs, either within the shaft or epiphyses of a bone or under the periosteum, especially in the following positions: the upper end of the tibia, the lower end of the femur, the upper end of the humerus, on the outer surface or within the lower jaw—constituting one form of malignant epulis—or in the antrum. When growing under the periosteum it is surrounded by a fibrous capsule only; but when in the centre of the bone it invades and expands the bone, until this may become so thin that it crackles under pressure of the fingers.

Naked-eye appearances.—It grows slowly, and may attain a considerable size, is moderately firm, fleshy, or elastic, pinkish or brownish yellow in colour, and on section has a peculiar “fasciculated” or sometimes a marbled appearance. The peripheral or growing part, in which small fragments of bone may often be found, is usually more pink than the centre, which is pale or brownish yellow, almost fatty looking, and variegated with brown or red patches (hæmorrhages of various ages), whilst at certain points are cysts containing a yellow or brown gelatinous material (derived from softened

tumour tissue stained with altered blood pigment). The hæmorrhages and cysts are very common as the vessels are numerous, embryonic in structure, and from the exposed position of the tumour and the unyielding nature of the structure on or in which it grows, especially liable to injury from external violence.

Harden (§ 62 or 63), stain (§§ 103 or 110 (*b*) and 132), and mount (§§ 193 and 199).

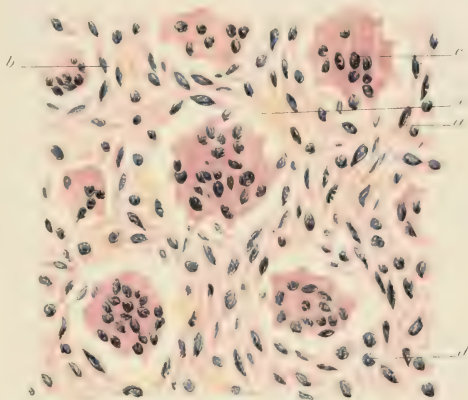


FIG. 240.—Myeloid or giant-celled sarcoma. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

- a.* Spindle cells, of which the tumour is principally composed.
- b.* Cells arranged to form the walls of embryonic blood-vessels.
- c.* Giant cell, with large number of nuclei scattered throughout its protoplasm.
- d.* Transverse sections of spindle cells.
- e.* Extravasated coloured blood corpuscles—escaped from ruptured vessels.

($\times 50$).—The bundles of small spindle cells, well developed, and cut in various directions, are readily observed. Throughout the section are small granular masses (collections of coloured blood corpuscles). The giant cells, more or less numerous, are seen as areas of protoplasm, about the size of a pin's head, delicately stained, with small deeply stained specks (nuclei) scattered through them. The delicate lines indicating the position of the blood vessels are very numerous.

($\times 300$).—Examine the spindle cells. The description of those in

the small spindle-celled sarcoma applies in this case also. The blood vessels are exceedingly numerous, and are composed simply of tumour cells, more or less regularly arranged in rows, between which the coloured blood corpuscles have pushed their way. Around these embryonic blood vessels masses of extravasated blood are frequently met with, the red blood corpuscles with their double outlines lying in direct contact with both spindle-shaped and giant cells. Here again there is little intercellular substance.

The giant or myeloid cells resemble very closely the osteoclasts of bone. They are large irregular masses of delicately tinted protoplasm, in which are imbedded twelve, twenty, or more, deeply stained nuclei massed near the centre or scattered irregularly throughout them. In many cases these cells are vacuolated.

Although this is the typical form of the giant-celled sarcoma, it must be remembered that these giant cells may be met with in any sarcoma which is growing in connection with bone, so that their presence must be looked upon simply as an accident of position of the tumour. Granules of altered blood pigment may usually be seen. In the yellow patches above described many of the spindle cells are becoming granular and fatty, the myeloid, like the round-celled, sarcomas frequently undergoing fatty degeneration.

The typical form seldom gives rise to secondary growths; but secondary tumours when found in the position ordinarily affected contain no giant cells; they are simply small spindle-celled sarcomas.

LARGE SPINDLE-CELLED SARCOMA

458. This form, though not absolutely distinct from the small spindle-celled variety, differs from it in many respects, both clinically and pathologically. The primary growth occurs in the same positions, but is found especially in the skin. It seldom reaches a very large size, but its growth may be extremely rapid; it is often very malignant and infects locally, and gives rise at a comparatively early stage to secondary growths in the lymphatic glands, followed, rapidly, by growths in other glands, and in the lungs, liver, intestine, brain, pleura, and pericardium.

Naked-eye appearances.—The tumour is softer, pinker, and more vascular than even the small spindle-celled form, and hæmorrhagic patches and soft gelatinous cysts similar to those found in the myeloid sarcoma are of frequent occurrence.

Harden (§ 60, 62, or 63), stain (§§ 102, 103, or 110 (*h*), and 132), and mount (§ 195 or 199).

($\times 50$) and ($\times 300$).—The cells are three or four times as large as are those of the small spindle-celled sarcoma. They are more like the ordinary fibro-plastic cells (the organising cells in a healing wound), but have between them little or no intercellular substance or formed material. They are very irregular in shape, are frequently bifurcated, and are arranged in bundles, the cells interlocking by their bifurcated ends. The blood channels between these cells are very numerous and of embryonic structure, and masses of extravasated blood are frequently seen. As some of the bundles are cut transversely, rounded sections, some nucleated, others without nuclei, are scattered over the field.

MELANOTIC SARCOMA

459. The most important of the large spindle-celled sarcomas is the melanotic or pigmented sarcoma, which grows especially from the choroid coat of the eye, the skin, and the pia mater.

It is extremely malignant, secondary growths usually making their appearance whenever the primary growth has reached the size of a walnut. These secondary tumours may grow in any of the positions usually affected by sarcomas, especially those of the large spindle-celled and mixed forms, and are frequently deeply pigmented, though in some cases they are devoid of any colouring matter.

The special malignancy of this tumour is due to the fact that it extends not only locally and by the blood vessels, but also by the lymphatics. It appears to be most malignant when growing from the true skin, in which case secondary growths may be looked for in all the positions above mentioned, in the liver, and in the submucous tissue of the intestine, when the primary growth has reached the size of a filbert.

Naked-eye appearances.—The specimen of which a description is here given was a large fungating blue-black mass, measuring about $2\frac{1}{2}$ inches in diameter, projecting from the orbit, and growing from the choroid coat through the eye-ball at the upper margin of the cornea. It bled on the slightest touch. On section, the mass was deep brownish or blue-black at certain parts; at others it was slaty grey, whilst at others again it was almost white or pale pink. It was comparatively soft, and extremely vascular.

Harden (§ 62 or 64) and stain (§§ 102-104 or 110 (*b*) and 132).

($\times 50$).—Note the arrangement of the large spindle cells into an open concentric network, with, in some cases, numerous small round cells lying in the meshes. Remember also that some of the large cells are cut transversely, that they are frequently arranged in bundles, and that there may be bundles of fibrous tissue in the tumour. At certain points pigment may be seen, usually collected around the nuclei of the large spindle cells, but sometimes lying between the cells.

($\times 300$).—Examine the large spindle-shaped or branching cells of which the open network is composed; these may be seen in both

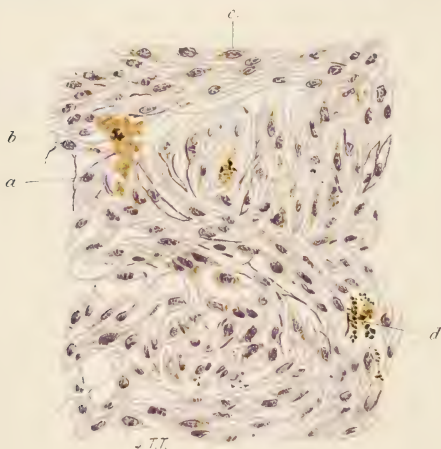


FIG. 241.—Melanotic sarcoma. Stained with logwood. ($\times 450$.)

- a.* Large spindle-shaped cell.
- b.* Branching cell.
- c.* Pigment around nucleus.
- d.* Pigment between cells.

Note the concentric arrangement of the cells, which at certain points form a kind of network.

longitudinal and transverse section; note also the large number of small round cells with which the meshes are sometimes crammed.

The embryonic blood vessels are surrounded by tissue which presents all the characters of lymphatic tissue. Around some of these vessels are small hæmorrhages, in which there may be altered blood pigment. This altered blood pigment must be carefully distinguished from the melanin proper, which is found as golden yellow or black granules, situated around the nuclei of the large spindle cells, more rarely in their protoplasm, and still more rarely in the spaces between the cells of the tumour. It is *not* derived directly from the blood pigment, but

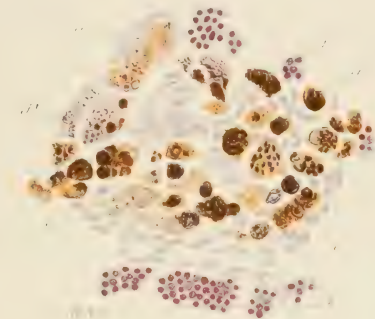


FIG. 242.—Melanotic sarcoma. Stained with logwood, and mounted in Canada balsam. ($\times 300$.)

- a.* Round cell distended with golden brown pigment.
- b.* Small round cells, unpigmented. Some of these may be spindle cells seen in transverse section.
- c.* Small spindle cells forming walls of embryonic blood vessels.
- d.* Multinucleated giant cells or plasmodia, one containing pigment the other without.
- e.* Spindle cell in which the pigment is collected around the nucleus.
- f.* Similar cell in which the whole protoplasm is crowded with pigment.

appears to be elaborated by the large cells of which the tumour is composed. When treated with dilute hydrochloric acid, and then soaked in a solution of potassium ferrocyanide, this pigment gives no blue reaction; but if a section be boiled in a solution of caustic potash, the pigment is dissolved, and a brown tinge, which immediately disappears on the addition of chlorine water, is given to the solution.

The pigment seen in old hæmorrhages, in brown induration of the lung and similar conditions, gives a blue reaction with hydrochloric acid and potassium ferrocyanide, whilst the coal pigment found in the lung gives no blue reaction, and is perfectly insoluble in boiling caustic potash.

In all sarcomas there may be various modifications of structure, and all kinds of combinations of the cells, in form, number, and arrangement, may be met with, and therefore all sarcomas do not present the regular or typical appearances above represented. Where the mixed sarcomas occur, they are both locally and generally malignant, and frequently appear to be developing into one of the higher or more specialised connective tissues. This, however, always stops short of full development.

ALVEOLAR SARCOMA

460. In the alveolar sarcoma, first described by Billroth, groups of sarcoma cells are arranged in alveoli formed by connective tissue, something like the alveoli in carcinoma, the only difference being that in this case we have cells of the connective tissue type instead of epithelial cells. It grows, usually, as a small tumour, possessing most of the characteristics of the ordinary sarcoma, in the true skin, and in the pia mater, muscle, and bone.

Harden (§ 60, 62, or 63), stain (§§ 102–104 or 110 (*b*) and 132), and mount (§§ 195 and 199).

($\times 50$) and ($\times 300$).—This sarcoma, at first sight, resembles a carcinoma. The cells are of considerable size, and are almost epithelial in character. They are large and rounded, may have a couple of nuclei, each of which has several deeply stained nucleoli. In consequence of the arrangement of pre-existing and newly formed vessels, these cells are divided into groups. Along with the blood vessels is a quantity of fibrillar tissue, which extends in some cases in delicate strands between individual cells, “but no vessels enter the cell groups” (Ziegler). The tumour is formed from lymphomatous tissue, in which the proliferation of the endothelial cells takes place rapidly without any corresponding increase in the stroma, the vessels and reticulum forming the thicker bands and more delicate stroma running between the groups of cells. The vessels are increased in number as the endothelial cells proliferate. Ziegler describes a similar

process in the tissues of the subarachnoid space and pia mater, where, he says, the masses of cells are formed from the endothelial covering of the trabeculae, the cells proliferating and forming thicker and thicker investing layers until the spaces are completely filled. This growth might be described as a lymphadenoma, with but a small formation of fibrillar tissue, in which sense it is an endothelioma (as distinguished from an epithelioma) and a true sarcoma.

461. An *angio-sarcoma* is a pulsatile tumour in which the whole mass appears to consist of embryonic blood vessels. The process of development of blood vessels is exactly similar to that already described in other sarcomas, but is carried a step further.

PSAMMOMA OR ANGIOLITHIC SARCOMA

462. This tumour grows from the inner surface of the dura mater, from the pia mater of the cerebrum or cerebellum; in the fringes of the choroid plexus; and in the brain substance or the pineal gland. They occur as small rounded tumours, often pedunculated or rough or nodular, and vary somewhat in consistence, usually being softer when they grow from the pineal gland or the cerebral substance.

Harden (§ 59 or 62), stain (§§ 103 or 110 (*b*) and 132), and mount (§ 199).

($\times 50$).—Note the well-defined fibro-cellular tissue in which run fairly numerous blood vessels. Penetrating this tissue are concentric layers of endothelial cells; in the centre of these processes the so-called brain sand may be seen. This appears to consist of laminae of colloid cells, in some of which lime salts are deposited. These brain sand centres may be in a single piece or they may be composed of several; they may be rounded, or they may be angular and irregular in shape.

($\times 250$).—Confirm the above features, and note especially the remains of the endothelioid cells at the margins of the colloid and cretaceous masses.

Local infiltration of the surrounding tissues has been described. In some cases similar growths are covered by more fully formed connective tissue; in these cases they are undoubtedly non-malignant.

A similar tumour is the cholesteatoma, which occurs, usually, in the

central canal of the spinal cord or in the mastoid and frontal sinuses. It consists of rounded masses made up of cells concentrically arranged

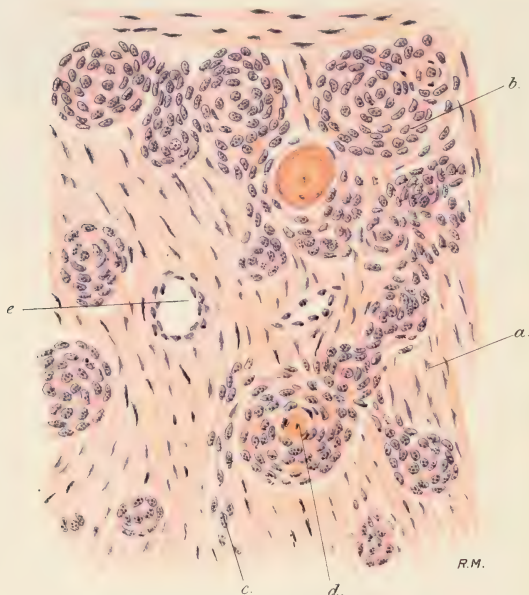


FIG. 243.—Section of a psammoma infiltrating the dura mater. Stained with alum hæmatein and picro-erythrosin. ($\times 300$.)

- a.* Dense fibrous tissue of the dura mater.
- b.* Concentric layers of endothelial cells invading the fibrous tissue.
- c.* Flattened layers of similar cells.
- d.* Concentric layers of endothelial cells with colloid mass in centre.
These may become infiltrated with calcareous material.
- e.* Blood vessel.

around collections of cholesterin crystals, crystals of fatty acids, etc., evidently derived from shed and degenerated epithelium.

OSTEO-SARCOMA

463. In the osteo-sarcoma, properly so called, there is an actual formation of true bony spicules, not only in the primary tumour but

also in the secondary growths. These tumours vary very much as regards the size and shape of the cells of which they are built up, but in all cases they grow in connection with bone, first as ordinary malignant sarcomas. They spread by the blood vessels, and secondary



FIG. 244.—Osteo-sarcoma stained with picro-carmin. ($\times 80$.)

- a.* Embryonic blood vessels.
- b.* Sarcoma cells.
- c.* Pink bony matrix, as yet, apparently, fibrous.
- d.* Cells lying in the fibrous matrix.
- e.* Cartilage cells with surrounding matrix. Transformation stages very well seen.

growths soon make their appearance in other bones, the characters of the primary tumour being reproduced.

On section, small hard but delicate spicules, which may be cut through with a knife, are met with.

Harden (§§ 62-64), stain (§§ 102-104, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—The softer parts are composed entirely of cells, round or spindle-shaped, as the case may be. At certain points bands of pink fibrous-looking tissue may be seen pushing their way between the masses of cells, showing that the matrix is becoming fibrous. Small green patches, bone, are also seen. In these patches or spicules we have regular lamination, Haversian canals, and all the essential features of true ossification (§§ 376 and 377).

($\times 300$).—The tumour cells take the place of the osteoblasts in this bone, otherwise the spicules are in all respects like those in true cancellous bone. In the neighbourhood of these growing centres of ossification the cells are modified, and many have assumed the characters of cartilage cells embedded in spaces bounded by capsules, and surrounded by the pink matrix. Later these tissues seem to become impregnated with lime salts, just as in growing and developing normal bone.

OSTEOID SARCOMA

464. This is a very malignant form of sarcoma, in which there is calcification but no true ossification. It grows primarily from the periosteum, and gives rise to secondary growths in serous membranes, the lungs, and other organs.

Harden (§ 60, 62, or 63), stain (§§ 102–104, or 110 (*b*), and 132), and mount (§§ 195 and 199).

($\times 50$).—Note that there is an increase of the intercellular substance, and that the cells are considerably larger than those of a small round-celled sarcoma, and are often multinucleated.

($\times 300$).—Between the large rounded multinucleated cells is a translucent delicately stained intercellular substance; at certain points, especially near the newly formed blood vessels, this material is infiltrated with dark or highly refractile calcareous particles. Where the calcification is very marked, the section gives a green reaction with picric acid. True bone structure is entirely wanting, and the hardness from which the tumour derives its name is due to the calcification of the cartilaginous matrix.

DEGENERATIONS AND MODIFICATIONS OF STRUCTURE OF SARCOMAS

465. (1) Fatty degeneration of the cells is due to imperfect nutrition; the cells first become granular, and then may break up altogether.

This is readily recognised, even with the naked eye, as the degenerating patches of the tissue become cream coloured or yellow.

(2) Hæmorrhagic degeneration from rupture of the embryonic blood vessels; this is often accompanied by the so-called cystic degeneration due to softening and then absorption of the softened and infiltrated tissues described in myeloid sarcoma (§ 457).

(3) Hyaline degeneration, especially of the cells in the immediate neighbourhood of the blood-vessels, gives rise to the formation of a kind of hyaline covering for the vessel.

(4) Myxomatous degeneration of the cells. The tumour becomes mucoid, and, on microscopic examination, clear mucoid globules are seen in the swollen cells. This must be carefully distinguished from mucoid softening of the intercellular substance.

The following are modifications of structure rather than true degenerations:—Fatty infiltration of the cells (lipomatous sarcoma); pigmentation of the cells, as in melanotic sarcoma. Myxomatous softening, calcification or chondrification of the intercellular substance also occur.

CANCEROUS OR MALIGNANT EPITHELIAL TUMOURS

466. For convenience of description, the epithelial tumours may be grouped as belonging to a class in which there is "growth of some or all tissue elements in excessive degree and erratic form, in which there is great vegetative power" (or power of growth as distinguished from functional activity), "the members of which are highly parasitic and malignant, infecting locally by direct transport, and through lymphatics and blood vessels. Secondary growths may affect any tissue" (Greenfield).

These tumours usually involve the mesoblast, but, unlike the sarcomas, they depend for their specific characters upon the epithelium developed from epi- or hypo-blast tissues. The above definition will, to a certain extent, cover the whole group: but there are slight modifications of structures in different species.

EPITHELIOMA

467. The first of the epithelial tumours to be considered is the epithelioma proper, in which the principal factor is an excessive and

irregular growth of epithelium. The epithelial masses invade the subjacent tissues by the lymphatic system, and secondary growths result in the lymphatic glands and other parts.

There are two forms: (1) Squamous-cell epithelioma; (2) columnar-cell epithelioma, according as they originate on a surface covered with squamous or with columnar epithelium.

(1) SQUAMOUS-CELL EPITHELIOMA

468. This occurs usually at the points of junction of the skin and mucous membrane, or at those parts which, from their movement and position, are exposed to considerable irritation, and where the epithelium is in a state of great proliferative activity—the lips, tongue, mouth, pharynx, œsophagus, in old scars and at the margin of chronic ulcers, orifice of vagina, rectum, and penis; from the hair follicles of the skin, and even from follicular cysts and dermoids, and from papillary warts and nævi.

Naked-eye appearances.—When fully developed, an epithelioma is an irregular warty-looking mass, the surface of which is ulcerated, and has an extremely characteristic appearance, generally compared to that of a cauliflower, from the prominence of certain small white points and ridges. From this surface an irritant watery or ichorous fluid exudes. The ulceration takes place only over the more or less rounded main mass of the tumour. At the margin of the central mass there is great induration, whilst surrounding it, but at some little distance, are numerous small firm nodules, each of which is distinctly marked off from the surrounding tissues. On scraping the ulcerated surface with a knife, small white points come away as rounded pellets, leaving behind them distinct pits or depressions. Press one of these pellets between two glass slips, and examine it in neutral solution (§ 36, 5); it is found to consist principally of large flattened epidermic scales, which stain yellow with picric acid.

On section the tumour tissue is firm, and running through the mass, bounding the white or yellowish masses of epithelium, are white glistening fibrous bands; as one would expect from the fact that hæmorrhages are extremely rare, there are very few blood vessels near the surface. These tumours may, however, ulcerate into one of the large vessels, and so give rise to fatal hæmorrhage.

Harden (§ 60, 62, or 72), stain (§§ 102–104, or 110 (b), and 132).

($\times 50$).—Examine first the ulcerating surface of the tumour, especially near the margin, where there will be noticed an extraordinary development of squamous epithelium, which, instead of merely clothing the papillae, grows downwards for some distance into the subjacent tissues in finger-like processes, which, in turn, send out secondary processes. Around these hypertrophied masses of epithelium there appears to be a considerable increase in the number of small round cells in the connective tissue, and although the vessels do not come near the surface, because of the thick layer of epithelium, in this

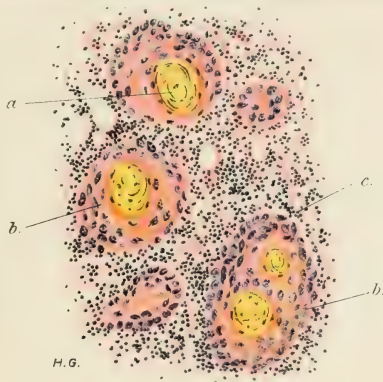


FIG. 245.—Epithelioma of the tongue. Stained with alum hæmatein and picro-erythrosin. ($\times 50$.)

- a.* Colloid centre of epithelial globule or "cell nest."
- b.* Flattened layers of cells around these colloid centres, which are composed partly of horny squames, such as are met with in the stratum corneum of the normal skin.
- c.* Small-celled tissue, very characteristic of the epithelioma.

subjacent tissue they are often of considerable size. In the still deeper tissues the masses of epithelium are seen running in all directions, each mass being surrounded by the cellular connective tissue. At certain points in these masses of epithelium are areas evidently composed of strata or layers of flattened cells; the centre of each mass is almost homogeneous. These are the cell nests so characteristic of this form of epithelioma.

($\times 300$).—The epithelial cells of which the penetrating columns are composed are in all respects like those found on a cutaneous surface.

The rete Malpighii and stratum corneum can be readily distinguished, and it is to this fact that the tumour owes its characteristic appearance, especially near the surface. The germinal layer and the prickle cells are also easily distinguished, the stratum granulosum and stratum lucidum not so readily. The horny layer is frequently very well developed, especially in the cell nests, which are seen to be composed of concentric layers of flattened cells arranged around a central colloid mass. In order to understand the method of formation of these cell nests, it must be remembered that, as in the normal skin, the epithelial cells are removed from the germinal layer; they gradually become dry and flattened, and lose their nuclei; these form the horny layer, and are then shed. In the epithelioma, as the cells grow in the pits they are removed from the germinal layer on the walls and are carried to the centre of the "shaft," where, as they cannot be removed as on a free surface, they undergo colloid changes, form a hard centre or core against which succeeding layers of cells are projected and flattened, and the peculiar laminated cell nests are the result.

Notice that near the surface, or where the epithelial projections have not passed for any great distance into the lymphatics of the corium, there are few round cells in the connective tissue, but that where the prolongations have extended further, the round cells become more numerous, the vascularity of the tissue in such cases becoming greatly increased. In the secondary growths the epithelial masses are usually growing more rapidly, have prickle cells well developed, but no horny layer, and are surrounded by more of the new round-celled tissue, though in certain cases there appears to be an entire absence of such tissue.

Squamous-cell epithelioma grows slowly, and, like all cancerous tumours, spreads by the lymphatics, though it is not very malignant. Extension along the nerves is not, by any means, common. When secondary growths occur, they are found first in the lymphatic glands, where they frequently cause superficial ulceration; after this they may be found in almost any position.

Epithelioma is distinguished from papilloma by the fact that the epithelium, in place of remaining in its normal relation to the subjacent corium and connective tissue, invades these structures by the lymphatic spaces; when this occurs the growth becomes malignant, the vegetative power of the epithelial growth increasing rapidly.

The varieties of epithelioma are due almost entirely to the rate of

growth and position of the tumour; it is therefore unnecessary to enter into any detailed account of them, but it must be remembered that where the tumours are of slowest growth, the cell nests are most



FIG. 246.—Section of the tongue of an old man, in which epithelium is growing down into the deeper tissues as in epithelioma. Stained with picro-carmin. ($\times 100$.)

- a.* Horny layer of the cuticle.
- b.* Clear and granular layers of epithelium.
- c.* Layer of columnar or germinal cells.
- d.* Mass of epithelium invading the lymph spaces of the deeper connective tissue.
- e.* Connective tissue basis of true skin; at *f.* somewhat more cellular.
- g.* Small vessel in the centre of a papilla of the corium.

perfectly formed, and that where the growth of the epithelial columns is very rapid, the cell nests may be absent, especially in the case of secondary growths.

469. A peculiar form of squamous-epithelial cancer endowed with little malignancy and which when removed does not return is often



FIG. 247.—Section of rodent ulcer. Stained with hæmatein and eosin.
($\times 60$.)

- a.* Ulcerating surface of epithelial mass. Cells smaller and rounder than in epithelioma.
- b.* Hair with surrounding "sheath," the layers of the outer root sheath well seen.
- c.* Invading cells. Opening of sebaceous gland.
- d.* Sections of sweat-gland tubes.
- e.* Alveoli of the sebaceous glands.
- f.* Small polygonal cells of tumour, growing from cells very similar to those seen in the outermost sheath of the hair. Invasion of cells well seen.
- g.* Proliferating connective tissue cells.
- h.* Section of blood vessel in corium.

found on the scalp, in the skin of the upper part of the face, on or near the eyelids, especially at the outer canthus, and at the angle of the nose, but rarely on the lips and chin, and more rarely on the upper

parts of the trunk or limbs. It is seen as a spreading ulcer, extending at one side but cicatrising and being covered with epithelium at the opposite margin. Although it spreads locally and in the early stages superficially, it may cause great destruction, sometimes extending to a considerable depth. This ulcer (Rodent ulcer) spreads somewhat irregularly, and although it is classified as a superficial carcinoma of the skin it is certainly not a very malignant growth. The edges of this slowly growing ulcer are usually slightly thickened and markedly overhanging; there is, as a rule, no secondary growth in the neighbouring lymphatic glands.

Harden (§ 62 or 64), stain (§ 103 or 104), and mount (§ 199).

($\times 50$).—Immediately under the epithelial surface and apparently taking their origin from the epithelium, not of the surface but of the sebaceous or sweat glands or from the external root sheath of hairs, note flask-shaped or irregular processes of epithelium projecting into the subcutaneous connective tissue. At the margin of such a process the cells are distinctly cubical and form a kind of germinal layer. The epithelial cells are comparatively small, and their nuclei deeply stained; the surrounding subcutaneous connective tissue may appear to be slightly more cellular than usual, but this is not by any means a very marked characteristic, there being no definite zone of small celled infiltration bounding the epithelial growth as in squamous epithelioma. There are neither cell nests nor any horny scales or colloid cells to be seen.

($\times 300$).—Verify the above features, and notice that the rounded or cubical epithelial cells with their well-stained nuclei are only about one-third the size of the cells seen in squamous epithelioma. The cells are ovoid, more regular, and frequently vacuolated.

(2) COLUMNAR-CELL EPITHELIOMA

470. The columnar-cell epithelioma, also termed, with almost equal accuracy, malignant adenoma and adenoid cancer, is found, in structure, to occupy an intermediate position between the simple adenoma and the true cancer, and also to bear the same relation to a papilloma of the intestine, say, that a squamous-epithelial epithelioma bears to a cutaneous papilloma.

It may be considered that the invading epithelium, in place of being squamous, is columnar or cubical; that hollow, finger-like

processes of epithelium branch or bud, and project into the subjacent tissue, where they are seen lining spaces with a distinct layer of columnar epithelium, which in some cases proliferates, and becomes more or less irregular. Sections of such a tumour have much the appearance of a true cancer of the encephaloid type (§ 473). Between the hollow epithelial prolongations a variable amount of fibro-cellular connective tissue is formed; this appears to be the result of an irritative overgrowth of the pre-existing connective tissue.

A similar structure is met with as a primary growth in the large intestine—especially at the flexures and in the rectum—as a soft, pale, succulent pinkish mass, the surface of which frequently ulcerates, projecting into the intestinal tube. When the surface of the cut section is scraped, a large quantity of opaque “cancer juice” comes away. It is so frequently situated at the lower part of the bowel that it is spoken of as the malignant polypus or adenoma of the rectum. It is also found in the stomach in a more diffuse form, where it is liable to undergo a peculiar softening, almost like that of colloid cancer, for which it may be easily mistaken; in the liver, beginning in the epithelium of the bile ducts; and in the lungs, being there developed, apparently, from the epithelium of the bronchial glands.

In the liver, columnar-cell epithelioma presents to the naked eye very much the appearances of true cancer. Scattered throughout the organ are a number of rounded or irregular masses, each of which has a characteristic appearance, the growing or peripheral part being much more vascular, softer, and more pink than the centre, where the tissue is yellower, and in some cases very fibrous. Small hæmorrhages are frequently met with. These masses, therefore, resemble scirrhus cancer in an early stage of development.

Harden (§ 65) and stain (§§ 102, 104, or 110 (*b*), and 132).

($\times 50$).—In the purest form, as seen in the rectum, there appears to be first an enormous increase in the size of the gland tubes in the true mucous membrane. From this point there is a gradual invasion of the deeper structures until the whole thickness of the intestinal wall is involved. Between the large irregular gland-like tubes or acini small-celled infiltration may be seen, at certain points only, as in the squamous epithelioma, especially in the deeper parts of the growth. Small outlying nodules of the glandular-looking tissue may also be observed.

($\times 300$).—Examine the tissue more fully. Each tube is lined with

a layer of regular columnar epithelium, the nucleus being usually placed



FIG. 248.—Malignant adenoma of the rectum, invading the whole of the tissues of the wall. Stained with alum hæmatein and eosin. ($\times 12$.)

a. Normal mucous membrane.

b. Tumour tissue on the mucous surface invading in turn (*c.*) the submucosa, (*d.*) the muscular, and (*e.*) the peritoneal coat of the rectum.

f. Cellular tissue in the immediate neighbourhood of the invading epithelium.

Note the large irregular alveolar spaces lined by a somewhat regular epithelium.

in the lower third of each cell. Beneath the well-formed epithelial

cells flattened cells may, in very good preparations, be recognised, but they appear to be very inconstant, even in number. Around some of the tubes, especially those near the surface, the stroma is like normal connective tissue, but in the deeper parts of the tumour, just as in the



FIG. 249.—Columnar-cell epithelioma (adenoid cancer of the stomach).
Stained with picro-carmin. ($\times 100$.)

- a.* Columnar epithelial cells.
- b.* Stroma, in which are numerous young connective tissue cells.
- c.* Alveolus.
- d.* Blood vessel in wall of stomach.
- e.* Muscular fibres from wall of stomach.

squamous-cell epithelioma, there is great increase in the number of small round cells.

In the lung the same features may be easily recognised, the tubules invading the lung substance in all directions.

In the liver, in the pink peripheral part of the tumour, the appearances are also very similar to those above described : but in the central

harder part there is an enormous increase of the stroma, which is more fibrous and contains comparatively few round cells. In consequence of this increase in the stroma, the gland follicles or tubes are more widely separated, and are much more irregular both in size and shape; in the tissue in the centre which is still older, the epithelium fills the spaces irregularly, and the lumen of the tubule is entirely obliterated. These points must be carefully kept in view when the growth and development of malignant adenoma and its relation to true carcinoma are under consideration.

CARCINOMA OR ACINOUS CANCER

471. The true carcinoma or acinous cancer consists of a system of connected alveoli or spaces, bounded by fibrous tissue—the stroma—these alveoli containing cells of an epithelial type. Embedded in the fibrous stroma, and quite separated from the epithelial elements, run *well-developed* blood vessels. The alveoli open into one another and are in direct communication with the lymphatics at the margin of the tumour. The classification usually given depends upon (1) the amount, nature, and arrangement of the stroma, and (2) the number and character of the cellular elements contained within the alveoli.

SCIRRHOUS CANCER

472. In the scirrhou or hard cancer the typical carcinomatous structure is well seen. The stroma, with well-formed blood vessels, is derived from the mesoblast; the epithelial cells are usually stated to be derived either from the epi- or hypo-blast. The alveolar structure is exceedingly well marked, the growth being slow and the fibrous stroma well developed.

Naked-eye appearances.—Scirrhou cancer occurs as a hard, firm tumour, varying somewhat in appearance, according to the position in which it grows—breast, pylorus, cesophagus, rectum, testis, ovary, kidney. In the breast it forms a hard, rounded mass, which is firmly attached to the subcutaneous tissue, very frequently causing retraction of the nipple. The section has a greyish-white, glistening, or silvery appearance, with, here and there, yellow patches. This appearance is due to the presence of hard fibrous bands, which run across and between small yellow masses of fatty tissue. In the centre of the

section, the retracting fibrous bands cause a depression, whilst the fatty masses project slightly above them. Near this centre are small patches of creamy or doughy tissue, the result of fatty degeneration of the older portions of the tumour. Towards the periphery the tissue is much more vascular, and assumes a pinker tinge and a softer consistence. Take a scraping from the margin of the tumour. It consists of a milky fluid, which mixed with water becomes slightly turbid. If a slice of this tumour be placed in a 5 per cent. watery solution of nitric acid and then washed in water, the fibrous bands and tissue throughout become gelatinous or translucent looking, the epithelial areas becoming distinctly opaque. For rapid diagnostic purposes this reaction is very valuable.

($\times 300$).—A number of cells, irregular in shape when isolated, and usually smaller than ordinary epithelial cells, are seen. Each is surrounded by a cell wall, and has a distinct nucleus in which nucleoli are easily distinguished. A scraping taken from the fatty centre is creamy and more opaque, and is made up of small shrivelled angular cells filled with small oil globules and granules; these cells are epithelial in type, and are undergoing marked fatty degeneration.

Harden pieces of both the peripheral and central parts of the tumour (§§ 60 and 62 or 71), stain (§§ 102, 103, 104, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—In the section taken from near the periphery, the tissue is composed of two sets of structures—first, connective tissue; and second, epithelial elements. The connective tissue is so arranged that it bounds a series of rounded or irregular spaces or alveoli, in which the epithelial cells are collected. In this section the stroma is partially fibrous, but at certain points there are great accumulations of deeply stained cells. These occur most frequently near the margin of the tumour, and form the cellular tissue into which the epithelial masses project; wherever the stroma is young and growing, these small cells are present in considerable numbers. They are young connective tissue cells, and of them the outer margin of the tumour is almost entirely composed. In these bands of stroma the well-developed blood vessels, quite separated from the epithelial masses, are readily distinguished. Although the bands of fibrous stroma are well marked, they are not nearly so thick and dense as are those near the centre of the tumour. The alveolar spaces are filled with angular cells, tolerably regular in shape, and closely packed.

($\times 300$).—Note the fibrous and cellular elements of the stroma; the position of the blood vessels, embedded in the fibrous bands; the cellular tissue, in which are no alveoli and no epithelial cells, at the margin of the tumour; and lastly, the angular cells which lie crowded together in the alveoli. The protoplasm is stained fairly distinctly, the large nucleus, in which nucleoli and vacuoles may be seen as deeply stained points and small clear spaces, is neither so deeply stained nor so clearly seen. There is no intercellular substance, or, at most, only a small quantity of fluid material.

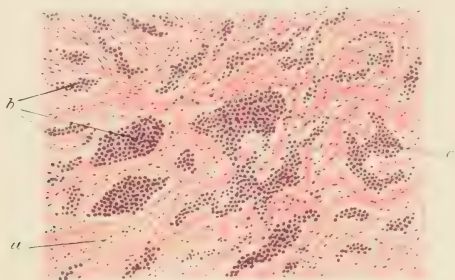


FIG. 250.—Scirrhus cancer of the breast. Stained with picro-erythrosin and van Gieson's stain. ($\times 50$.)

- a.* Fibrous stroma, in which run well-formed vessels.
- b.* Alveoli, containing
- c.* Epithelioid cells.

To further examine the alveoli, and to determine their communication with the surrounding lymphatics, a thin section of the tumour taken from near the growing margin should be treated at once with nitrate of silver (§ 137), and then mounted in glycerin (§ 194).

In the section from the central part of the tumour ($\times 50$ and $\times 300$) it may be observed that the fibrous stroma has become exceedingly dense, and in some parts constitutes almost the entire mass of the tumour growth. The alveoli are much smaller than those already examined, and contain only a few shrivelled atrophied and

angular cells. These epithelial cells have undergone fatty degeneration, and the greater part of them have evidently been absorbed, as the stroma has become more dense, but less vascular. As the stroma comes to predominate more and more, it becomes more fibrous and cicatricial, and, like all cicatricial tissue, tends to contract. The contracting fibrous tissue drawing upon the nipple, or upon the tissues

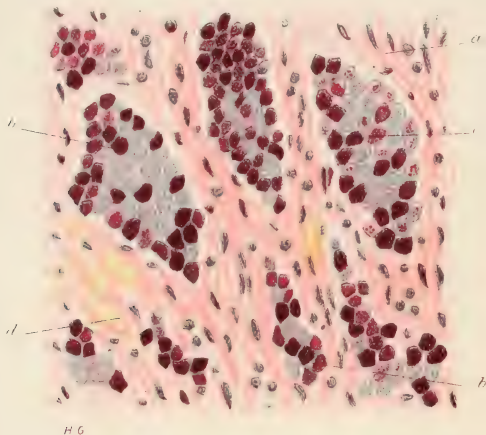


FIG. 251.—Scirrhus cancer of the breast. Stained with alum hæmatein and van Gieson's stain. ($\times 300$.)

- a.* Fibrous stroma bounding
- b.* Alveoli.
- c.* Epithelioid cells, some with several nuclei. Note the irregular shape and epithelial character.
- d.* Blood vessels supported by well-formed fibrous tissue.

around the centre of the tumour, gives rise to a retraction of the nipple—umbilication—which is such a characteristic feature of all scirrhus cancers.

ENCEPHALOID CANCER

473. Under this heading come all those soft, rapidly growing, brain-like or medullary cancers, in which the stroma is very scanty, the alveoli large, and the cells large and numerous.

Naked-eye appearances.—The primary encephaloid cancer grows

especially from the mucous membranes, testes, and breast; but as a secondary growth, following primary scirrhus cancer, it frequently grows in the more vascular organs. It occurs as soft, pale pink nodules, of various sizes and shapes, which, when scraped, yield a considerable quantity of opaque "cancer juice" (which contains large

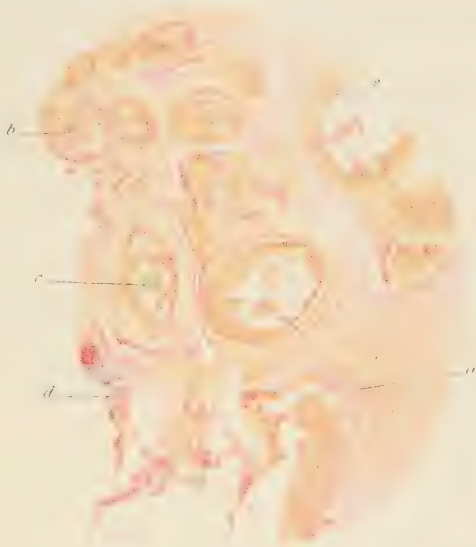


FIG. 252.—Section of encephaloid cancer of the breast. Stained with picro-carmin. ($\times 40$.)

- a.* Cellular connective tissue near advancing epithelium.
- b.* Well-marked alveolus filled with epithelial cells.
- c.* Colloid mass derived from cells which usually form milk.
- d.* Fatty tissue of breast.
- e.* Older fibrous band of stroma.

rounded epithelial cells with three or four nuclei, with nucleoli and smaller cells with a single nucleus). At the growing margins the tissues are more vascular, softer and pinker; in the centre the tissue is often more firm and fibrous in consistence and yellower in colour. Hemorrhages are frequently met with.

Harden (§ 65) and stain (§§ 102, 104, or 110 (*b*), and 132).

($\times 50$).—The stroma is exceedingly scanty, and in consequence the vessels, which are relatively numerous, are badly supported, though structurally they are usually well developed. The alveoli are large and very numerous, but vary greatly in size, and, with their contained epithelial cells, constitute the greater part of the growth.

($\times 300$).—The stroma is very delicate, and in many cases excessively cellular, supporting the blood vessels very indifferently. At some points there may be extravasations of blood from ruptured vessels, in which case the blood corpuscles find their way into the alveoli.

In the alveoli the cells present great differences both as to size and arrangement, according to the origin of the tumour. In some cases, where the cancer has its origin in a gland duct, the cells are large, almost columnar, arranged regularly near the wall of the alveolus, but grouped indiscriminately near the centre, the arrangement, in this instance, resembling that of the malignant adenoma. In other cases, when the breast is the seat of origin, the cells may be large and rounded, having three or four nuclei and nucleoli, or they may be polygonal or irregular in shape, like those found in the developing breast acini.

The cells of a cancer multiply by indirect division of the nucleus; a process which may be very readily followed in this tumour.

COLLOID CANCER

474. The colloid cancer may be looked upon as one of the forms of cancer already mentioned, in which the epithelial cells have undergone colloid degeneration. It is especially common in the gastrointestinal mucous membrane, in the abdominal cavity, in the breast and ovary, and more rarely in other viscera.

Naked-eye appearances.—The presence of the colloid change is indicated by a peculiar brownish glue-like or gelatinous appearance. When the growth is diffuse, and occurs in a serous membrane, as in the peritoneum, it may form a gelatinous mass which appears to form a coating over the whole of the abdominal organs, like a gelatin cast of the viscera. In colloid cancer of the breast, the degeneration takes place in portions only which have the same peculiar gelatinous consistence.

Harden (§ 60, 63, or 65) and stain (§§ 102 or 104 and 167).

($\times 90$).—The stroma differs in no respect from that in one or other

of the forms previously described, except perhaps that it is more open and somewhat cellular; but the alveoli are more rounded. The cells within these alveoli may be so altered that it is sometimes difficult to make them out: usually, however, a few nucleated epithelial cells may be seen lying in a gelatinous-looking mass. On staining by Weigert's method (§ 167), this gelatinous-looking mass is seen to contain a number of fibrils which take on a deep blue colour, but the bulk is

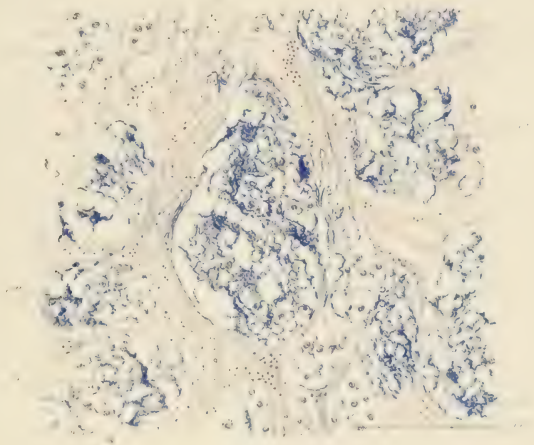


FIG. 253.—Section of colloid cancer from the pyloric end of the stomach. Stained by Weigert's method. ($\times 90$.)

a, a', a''. Alveolus containing epithelial cells.

b, b'. Stroma in which some proliferation may be seen.

c, c', c''. "Colloid" material derived from the breaking-down
"cancer cells."

evidently derived from the degeneration (colloid) of the epithelial cells. This colloid material may infiltrate the connective tissue stroma, which, in turn, has a peculiar mucoid appearance, and certainly gives somewhat different staining reactions from the colloid in the cells and infiltrating the connective tissue.

($\times 300$).—Confirm the above, and in a section of colloid cancer of the breast stained with picro-carmin (§ 102), note that where the cells are not entirely replaced by colloid material, they are swollen and

rounded, and contain yellow drops or globules. In some cells the protoplasm forms a mere film around the colloid globule, and eventually even this may disappear, the globule joining the main mass of colloid. In other cases a few altered and swollen cells may be left in the centre of the colloid material. In the breast, this substance often penetrates between the layers of fibrous tissue forming the wall of the alveolus,

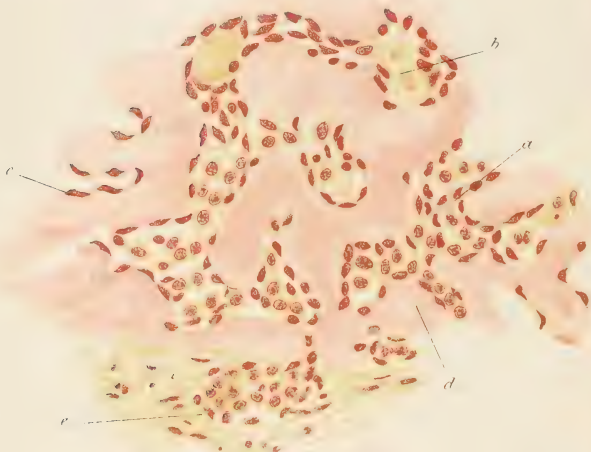


FIG. 254.—Section of colloid cancer of the breast. Stained with picro-carmin. ($\times 300$.)

- a.* Epithelial cells filling alveolus.
- b.* Epithelial cells undergoing colloid degeneration.
- c.* Flattened cells covering fibrous trabeculae.
- d.* Swollen homogeneous mucoid (?) fibrous tissue.
- e.* Normal stroma.

giving a more characteristic appearance even than in the peritoneal tumour; these layers stripped off one after the other by the invading colloid material form a peculiar laminated mass, which is made up as follows:—In the centre are the altered cells, surrounding them is the colloid material, and around this again are successive alternate layers of fibrous tissue and colloid.

From the above description of the various forms of cancer it will be

understood that they are all of an exceedingly malignant character. The encephaloid cancer is most malignant, the squamous epithelioma and rodent ulcer least so. They spread by the lymphatics both locally and to distant parts.

DEGENERATIVE CHANGES IN CANCER

475. These changes modify, in a very marked manner, both the naked-eye and microscopic appearances.

(1) Colloid and (2) fatty degeneration of the cells, and (3) myxomatous or mucoid degeneration of the stroma, have already been mentioned.

(4) A cancer may soften *en masse*, or superficially; this leads to ulceration, following fatty degeneration or necrosis. It occurs especially when the tumour is exposed to the action of irritant or digestive fluids, or to mechanical injury. Such ulceration is usually followed by hæmorrhage.

(5) Hæmorrhage also occurs, as already mentioned, in encephaloid cancers; it is frequently met with in *carcinoma telangiectodes* or erectile carcinoma, where well-developed vessels, on which are small dilatations, project from the stroma into the alveoli, and, being no longer supported, rupture, serious hæmorrhage resulting.

(6) Inflammation of cancerous growths is also very commonly found; the results are very similar to those met with in inflammation of any normal tissue—vascular changes and connective tissue proliferation.

(7) Pigmentation of the stroma of cancerous growths also occurs. Most of the so-called pigmented cancers, however, are nothing but melanotic sarcomas.

DIAGNOSTIC FEATURES OF SARCOMA AND CARCINOMA

476. The following points, arranged in tabular form, may prove helpful to the student who has examined carefully both the sarcoma and the carcinoma:—

SARCOMA	CARCINOMA
1. <i>Origin</i> Entirely mesoblastic. (Connective tissue.)	Meso- and epi- or hypoblastic. (Both connective and epithelial tissue.)

SARCOMA—*continued*CARCINOMA—*continued*

- | | |
|---|---|
| <p>2. <i>Stroma</i> . . . Intercellular. Rarely forms alveoli.</p> <p>3. <i>Cells</i> . . . Granulation tissue or embryonic connective tissue cells, not epithelial (shapes various).</p> <p>4. <i>Intercellular substance</i> } May be present.</p> <p>5. <i>Vessels</i> . . . Embryonic in character. They are in direct contact with, or rather are composed of, the special cells, slightly modified, of which the tumour is composed.</p> <p>6. <i>Spreads</i> . . . By blood vessels.</p> <p>7. <i>Malignancy</i>. Great.</p> | <p>Vascular connective tissue, which forms alveoli; these alveoli communicate with one another and with the surrounding lymphatics, and contain masses of epithelial cells.</p> <p>Epithelial cells contained within alveoli, shape and size various. Distinct nuclei and nucleoli.</p> <p>Absent, or merely fluid.</p> <p>Well developed, contained within and supported by the walls of the alveoli. Seldom in contact with the cells.</p> <p>By lymphatics, especially in nerves and around blood vessels, except in the later stages, when they may also spread by blood vessels; they then spread with very great rapidity. This occurs in vascular organs only.</p> <p>Greater.</p> |
|---|---|

PSOROZOA (?) IN CANCERS

477. During the last few years many observations have been made on the invasion of epithelial cells by certain forms of parasites. In some of the lower animal forms, namely, certain fish, the snail, the rabbit, etc., zoologists have demonstrated the presence of psorozoa, psorospermæ or coccidia; and from the nature of the changes set up in these cases, pathologists have been led to examine cancerous tumours for similar organisms.

That such organisms do exist in Paget's disease (demonstrated by Wickham), and even in epithelial tumours of various kinds, is strongly maintained by certain observers; and in order that those who are engaged in the study of cancer may prepare material in which they can see such bodies as have been described, it may be well to give a

short account of the methods employed by Russell and Soudakewitch in their several researches.

Russell hardens in the ordinary fashion (§§ 60-62) and stains (*vide infra*).

($\times 50$).—In a section stained by this method there may be seen in the epithelial cells, lying in the alveoli, single purple or fuchsin stained bodies, usually rounded and deeply stained, or groups or clusters of similar bodies which stand out very prominently from the greenish-blue epithelial tissue.

($\times 300$).—These bodies are in the protoplasm of the epithelial cell near the nucleus, and pushing it to one side, or in some cases actually within the nucleus itself. Seen under a very high power they appear to have a somewhat radiate structure, especially at the margin, but most of them, where the tissues have been hardened by any of the ordinary methods, are quite homogeneous. Sections prepared in this manner show also colloid masses in or near the epithelial cells; it is stated, however, that there are organisms that have undergone change owing to the slowness of the fixing process. A certain number of red blood corpuscles also take on this stain, unless the decolorising method is carefully carried out. Ruffer, Moore and Walker, and others have described similar structures, but the latter indicate that they are nothing but the archo-plasmic vesicles similar to those that occur during the mitotic division of the cells of the testes, *e.g.* in the guinea-pig.

Place the section in water, and then stain in a saturated solution, made by dissolving fuchsin in 2 per cent. carbolic acid water, for ten minutes or longer; wash for a few minutes in water, then for half a minute in absolute alcohol; from this put the section into a 1 per cent. solution of iodine green (Grübler's) dissolved in 2 per cent. carbolic acid water, and allow it to remain in this, well spread out, for five minutes; rapidly dehydrate in absolute alcohol, pass through oil of cloves, and mount in Canada balsam.

Soudakewitch, working at this subject, has been able to demonstrate structures which Metchnikoff declares can be nothing other than psorosperms or coccidia. Taking pieces from rapidly growing cancers in glandular structures Soudakewitch hardens for one or two days in 1 per cent. osmic acid (§ 69), or in Flemming's solution (§ 70), the tissue is then transferred to Muller's fluid, in which it is left for five days, then well washed in water for twelve or twenty-four

hours, and then passed through spirit of various strengths (§ 60). Stain (§ 109).

($\times 50$).—The organisms may be seen in much the same positions as described by Russell, as small homogeneous or granular stained bodies embedded in the epithelial cells in the alveoli.

($\times 450$).—It is difficult to distinguish the numerous forms described by Soudakewitch, especially in slowly growing cancers. At first sight they appear as rounded nuclei, some of them granular, others with a delicate network running through their substance, others again are like nuclei, with well-marked nucleoli, which in some cases are stained, in others unstained; but it will be observed that, just as in the fuchsin bodies, these rounded “psorosperms” are actually within the nucleus of the cell, or have pushed it to one side. Whether these “parasites” are the causal agents in cancerous infection, or whether they are simply associated with some special form of division, it is difficult to determine.

CHAPTER XV

ANIMAL PARASITES

TREMATODES

478. *Fasciola hepatica*, syn. *Distomum hepaticum*, or fluke of liver-rot in sheep, rarely occurs in man. It is found as a flattened leaf-like worm, one-half to three-quarters of an inch long, lying curled up in the bile ducts and gall bladder. When flattened out it is broader at the anterior than at the posterior end, and is prolonged into a narrow proboscis in front. It is brownish, with a pink tinge. To inject the worm, kill by plunging it into warm thin gelatin carmine, which is immediately taken into the alimentary canal. To preserve for examination soak thoroughly in glycerin, and mount in a deep cell in the same medium. With a hand-lens examine and note the oral sucker at the anterior extremity of the proboscis; from this runs the injected alimentary canal, which is deeply bifurcated and branched, giving off lateral diverticula, and ending in cæca. Behind the mouth is the genital aperture, and next to this comes the ventral acetabulum or disc; behind this again comes a convoluted tube—the uterus, occupying a considerable proportion of the body cavity. The testes are situated more centrally, and are bifurcated. The body is enclosed in a chitinous cuticle, which is covered with very minute spines. This organism, like many others of the animal parasites, is not developed completely in one host. In one it passes through certain stages of its existence, after which, unless taken up by a second host, it remains quiescent or dies. The first host (in which development is incomplete) is spoken of as the *intermediate* host; the second as the *final* host, and the parasite must gain access to both in order that it may pass through its full cycle of development or generation. The *intermediate* host of the *Fasciola hepatica* is the fresh-water snail *Limnea truncatula*; the following is its *cycle of generation*: ovum:

ciliated embryo, set free in water by the opening of an operculum; the embryo then loses its cilia and enters the intermediate host, where it becomes encysted. It then forms a sporocyst in which *redia* are formed by a process of internal gemmation. In the *redia* small-tailed embryos are formed—the *ceraria*: these escape, and after swimming in water by means of the muscular tail, encyst on grass and enter the final host with its food, and becoming sexually developed into hermaphrodite forms, lose their tails, and the cycle is repeated.

Dicrocoelium lanceatum a longer and narrower form of fluke, also occurs in man.

Schistosomum hæmatobium, *Bilharzia hæmatobia*, or blood-fluke, is an important member of this group, as it is present in the portal and splenic veins, and in the vessels of the mucous membrane of the rectum and bladder; by its presence in the latter position it sets up hæmaturia. It is met with especially in Egypt, the west coast of Arabia, Mauritius, and the Cape. Unlike the other trematodes, it is bisexual.

The male is about half an inch long, is somewhat flattened and curved in on its ventral surface, so that a transverse section is crescentic. Two discs, larger in the male than in the female, are placed near the anterior extremity, and the genital orifice lies behind the posterior of these. The female is about one inch in length, is filiform, and is received into the ventral groove and the *canalis gynæcophorus*, formed by a further folding in of the lateral margins at the posterior extremity of the male. In the urine from a case in which this parasite is present, a quantity of blood may usually be found. Sometimes, however, scarcely a trace can be detected with the naked eye. In the urinary sediment, examined under the microscope, large numbers of ova may be distinguished. These ova are about $\frac{1}{100}$ of an inch in length, are oval, and have a spine or beak situated, usually, at the broader end. They are yellow, transparent, and smooth; through the transparent investment the ciliated larva may be seen. If to the sediment containing these ova a few drops of hot water be added, and one of the ova be watched under a low power for a few minutes, a movement of cilia may soon be observed within the investing membrane. This becoming very active, the membrane ruptures. The released embryo has imperfectly developed organs, but darts about with great rapidity, the cilia working actively.

Stain (§ 102) and mount (§ 194), or better (§ 195).

Fasciolopsis buski, syn. *D. crassum*, found in the duodenum :
Opisthorchis sinensis, syn. *D. sinense*, and *Opisthorchis noverca*, syn. *D.*



FIG. 255.

- a. Ovum containing young embryo of *Schistosomum* and pus cell from sediment of urine from a case of *Bilharzia hamatobia*.
- b. Ovum with operculum of *Fasciola hepatica*.
- c. Ovum of *Opisthorchis sinensis*.
- d. Ovum of *Cotylagonimus heterophyes*.

All $\times 400$ in order that their sizes may be compared.

conjunctum, in the liver ; *Cotylagonimus heterophyes*, syn. *D. heterophyes* in the intestines,—are the other more important members of this group.

CESTODES OR TAPE-WORMS

479. Each tape-worm consists of a head and a series of segments or proglottides, each segment, however, with the exception of those situated at the anterior extremity of the chain, being sexually complete. The whole chain is termed a strobilus, the most anterior modified segment forming the head and neck ; after these come the proglottides or segments, first the sexually immature, and then the mature and hermaphrodite

segments. In this group alternation of generation is strictly maintained throughout. The fully developed form occurs in the alimentary canal of the final host, and must be looked for in the fæces, which must be carefully broken down with a stream of water, and strained through fine muslin, so as to intercept the various fragments of the strobilus.

TÆNIA SAGINATA

480. Syn., *T. mediocanellata*, *T. inermis*.—This is probably the commonest form in England and India, but not in Germany. The intermediate host, in which the cystic form (*Cysticercus bovis*) occurs, is the ox.

Naked-eye appearances.—In the cystic form it is found as small yellowish vesicles in the muscles, especially in the thin curved muscles of a round of beef, in the lungs, and in the liver.

The matured worm is a soft, flattened, yellowish white “band” or ribbon worm, which sometimes attains a length of over twenty feet.



FIG. 256.—Head and immature segments of *Tænia saginata* (natural size).

- a. Head with four suckers.
- b. Neck.
- c. Immature segments.

Examined under a low magnifying power, the head is seen to be square and somewhat flattened, about one-twelfth of an inch in diameter, having no beak or rostellum, or only a small proboscis, and no hooklets. At each corner of the head is a muscular sucker. Examine the fully matured proglottides, arranged in a continuous series. Small papillæ with central openings alternate irregularly on each side of the ribbon, a little below the centre of the segment. Running down each side of the flattened segments, which are square, or longer than broad, is a branch of the water vascular canal, whilst in the fore part of each segment runs a transverse connecting branch. By plunging the living worm into a warm solution of carmine, or carmine gelatin, a

most beautiful injection of the water vascular system may be obtained. The uterus is very much branched, some twenty to twenty-five primary branches being found, the diverticula branching dichotomously. The testis consists of a number of scattered testes, which ultimately open into a convoluted tube placed in the anterior part of the segment, from



FIG. 257.

- a.* Flattened head of *Tænia saginata*, with four suckers well seen.
 Neck becoming constricted. ($\times 30$.)
b. Ovum of *T. saginata*. ($\times 400$.)

which passes a duct ending in a cirrus or penis, which may in some cases be seen protruding through the genital pore; close to this is the opening of the vagina. Near the posterior part of each segment are paired ovaries and a vitelline or yolk gland. Each strobilus consists of three or four thousand segments, the sexually matured proglottides commencing at about the 450th from the head. To preserve these

worms for future examination, soak in glycerin and mount in a deep cell, or stain (§§ 102, 105, or 110 (*b*), and 132), clear up thoroughly (§ 193), and mount in a cell (§ 197). To mount as a permanent preparation, whilst still moist, arrange it in a series of concentric circles on a piece of clean glass. Begin with the head in the centre, and work gradually outwards; allowed to dry *in situ* the worm adheres firmly to the glass.

TÆNIA SOLIUM

481. Syn., *T. cucurbitina plana*, or *T. vulgaris*.—This is the form which occurs most frequently in Germany.

Naked-eye appearances.—The cystic form—*Cysticercus cellulosæ*—occurs in pork, where it gives rise to the so-called *measly* condition. A similar cystic form is met with, more rarely, in man, in the subcutaneous areolar tissue, between the muscles, in the eye and in the brain. Like the *T. saginata*, the strobilus is composed of head and neck, and proglottides. It is shorter than the *T. saginata*, but is several feet in length, and consists of about 1200 segments.

($\times 50$).—Around the head are four suckers arranged below a well-marked rostellum; this is armed with a double circlet of from 26 to 28 hooklets, the anterior row made up of larger hooklets than the posterior, but all considerably larger than those of the *T. echinococcus*. The water vascular system near the rostellum is like that met with in *T. saginata*—double, and may be injected in the same manner. The segments are square, or are longer than broad; the uterus has a number of lateral branches (seven to ten), which again subdivide, but not nearly to the same extent as in the *T. saginata*. The cirrus genital pores, which *alternate regularly*, should also be examined. Prepare as for *T. saginata*.

DIBOTHRIOCEPHALUS LATUS

482. Syn., *Tenia lata*.—This form of tape-worm, which is frequently met with in Iceland, Holland, North-East Germany, Geneva, Southern and Eastern Russia, and on the shores of the Caspian Sea, has its larval form in certain species of fish which are especially common in the regions mentioned. The bleak, according to Dr. Fock, quoted by Cobbold, is possibly the intermediate host, from which the parasite passes to the Dutch Jews. The pike, eel, trout, and pout are also mentioned in this connection.

Naked-eye appearances.—*D. latus* is the largest of the tape-worms occurring in man; it may be as much as twenty-five feet in length, and over half an inch in breadth. The head is about $\frac{1}{3}$ of an inch broad, is club-shaped, but slightly flattened; it has no rostellum and no hooklets: and running down each side is a very characteristic groove. Behind the head comes a thin neck, after which come the proglottides, three or four thousand in number. The earlier segments are extremely narrow and short; but as the segments become sexually matured (at about the 600th segment) they are broader and about one-eighth inch in length, whilst at the posterior extremity they again taper off slightly in breadth, but are as much as one quarter of an inch in length. The worm is flat and ribbon-like. The segments have a brownish tinge, and in the centre of each, or a little nearer the front on the ventral surface, is a



FIG. 258.—Ova (after Looss) of (a.) *Tænia solium*, with thick capsule and three pairs of hooklets, and (b.) *Dibothriocephalus latus*, with operculum (both $\times 400$ for purposes of comparison).

distinct, deeply pigmented elevation or thickening, in the middle of which is placed the genital pore. The pigmentation is due to the presence of numerous dark-coloured ova. The uterus lies in the centre of the segment, and forms a rosette-shaped mass. The testes are scattered. The water vascular system is similar to that of the other members of the group. For permanent preparations of the head or of the segments, stain and mount as for *T. saginata* (§ 480).

Cycle of development of tape-worms.—Beginning with the sexually matured segments, proglottides are voided from the intestine of the final host: ova are discharged or escape from these as they become disorganised. They are then taken up by the intermediate host, generally in water or on herbage, into the alimentary canal: here the ovum opens by an operculum, and an embryo, with three pairs of hooks, emerges and makes its way through the walls of the alimentary canal to the

muscles or liver, etc., increases in size, and becomes vacuolated, the hooklets disappear, a chitinous or horny cuticle is developed, and an imperfect water vascular system makes its appearance. The sac then becomes thickened at one point, and invagination of this goes on until a double-walled sac, open at one end, is formed. At the bottom of the sac, on the inner wall, hooklets are seen (if present in the tape-worm form), then elevations, which eventually form the suckers; this inner part of the floor, looking towards the mouth of the sac, is the head. All this takes place in the first or intermediate host. In some instances, as in the hydatid cysts to be afterwards described, a secondary or even a tertiary internal budding takes place, so that in the primary cysts a large number of scolices, or undeveloped heads, may be formed.

When the muscular or other tissue, with the contained encysted parasites,—measly pork, for example,—is taken into the alimentary canal of the second or final host, the cyst wall is dissolved by the gastric juice, the head becomes evaginated, attaches itself to the wall of the intestine, proglottides are developed behind it, and the cycle begins anew.

When man is the primary host, the “measles” are found in the positions before mentioned. A fibrous pseudo-cyst is formed around the cystic parasite, which may live for a considerable time. Should the cystic form die, however, the cyst becomes calcified, the contents undergo caseation and calcification, and the only evidence of the larva left are the hooklets, which may almost invariably be found in *T. solium*.

TÆNIA ECHINOCOCCUS

483. The *Tænia echinococcus*, or the tape-worm of the dog, is important only in that it gives rise to a cystic form in man, who is the intermediate host. It is a worm measuring about a quarter of an inch in length, one-half of the whole length being taken up by the terminal proglottis, the only one that comes to sexual maturity. The head is rather like that of the *T. solium*, but is smaller. It has a distinct rostellum, surrounded by a double row of hooklets, thirty or forty in number, similar in shape to those of the *T. solium* but only about one-third of the size. Here, too, as in the *T. solium*, there are four suckers which may readily be seen. There is a well-developed water vascular system; the genital pore is placed a little behind the centre of the

matured segment. The uterus occupies the greater part of the segment, and is filled with ova.

HYDATID CYST

484. The cystic form of the *T. echinococcus* occurs most frequently in the liver and peritoneum, but also in the lungs, spleen, heart, and pericardium, nerve centres and retina, kidneys, muscles, and subcutaneous tissues. In Iceland, according to Cobbold, "it is the cause of one-sixth of the annual mortality"; and in Switzerland, Southern Germany, and Australia (Victoria) it frequently occurs; it is more rare in England and Scotland.

Naked-eye appearances.—The cysts vary greatly both in size and number; they may be only the size of a pin's head or they may grow to several times the normal size of the organs in which they are developed. In some cases they are single, but in others there are several in the same organ, or there may be numerous cysts occurring simultaneously in several organs.

Examine one of the cysts. Before the organ is disturbed there is usually considerable bulging at the point where the cyst is situated (in the liver, most frequently on the upper surface of the right lobe). Make a crucial incision into the bulging part, cutting carefully through a fibrous capsule that is found, and reflect the flaps from the true cyst. This fibrous capsule or pseudo-cyst consists of new or compressed tissue, the new tissue being the result of pressure irritation of the connective tissue of the organ. The true capsule now exposed is white and opaque, almost like boiled white of egg, and from its outer surface, surrounding well-lighted objects, such as a window, are reflected. Open the capsule and remove some of the fluid. This has a specific gravity of 1004 to 1013; it gives no gelatinous or other precipitate with heat or nitric acid, and therefore contains no albumin. With nitrate of silver a white cloudy precipitate is formed, as the fluid contains about a half per cent. of sodium chloride. On the escape of the fluid the membrane curls inwards in a very characteristic fashion. If the fluid be set aside in a conical glass to settle, and some of the granular-looking sediment, mixed with Farrant's solution, be mounted in a shallow cell and covered with a cover glass, the scolices may be made out under the microscope.

($\times 50$).—The scolices appear to be about the size of millet seeds. Some of them are rounded, others are more elongated, and have at

one end a dark-coloured disc or zone. The body appears granular, and small suckers may be observed. A number of these small bodies

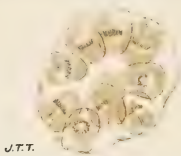


FIG. 259.—A number of scolices contained within a delicate brood capsule. Mounted in glycerin. ($\times 70$.)

Note the circlet of hooklets retracted within the body of each scolex.

may be grouped together and surrounded by a delicate membrane or brood capsule, which is attached to the endocyst.

($\times 300$).—The structure of the scolices may be further defined: the circlet of hooks; the suckers placed somewhat laterally; the body

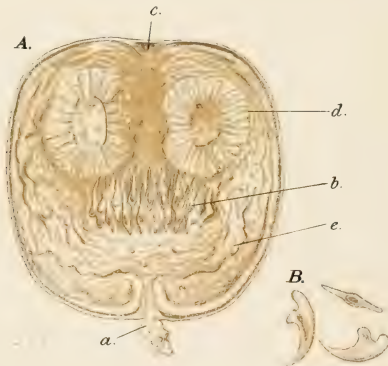


FIG. 260.—A. Drawing of *Echinococcus*. Head or scolex. ($\times 450$.)

a. Pedicle, by which the head is attached to the endocyst.

b. Circlet of hooklets.

c. Depression at the point of invagination of the anterior segment.

d. Suckers with radiating fibres.

e. Vascular canals (?).

B. Detached hooklets. ($\times 450$.)

containing the bright-looking globules and particles. A number of hooklets may usually be seen in any hydatid fluid, and these should be

carefully examined in order that they may be recognised, even after the contents of the cyst have undergone suppuration or other degenerative changes. Examine a scraping of the endocyst removed from the inner surface of the cyst, mixed with Farrant's solution, and pressed between two glass slips. It is found to consist of a granular mass, in which are imbedded the scolices, similar to those above described. From this endocyst or inner layer of the hydatid membrane are developed the scolices, or, where the primary cysts are of large size, the secondary cysts. As these secondary cysts grow, tertiary cysts may in turn be developed within them. These of course may be observed during the naked-eye examination.

The ectocyst, or thick white of egg-like outer layer, varies in thickness according to the size of the cyst. It is the curling inwards of



FIG. 261.—Laminated ectocyst of the true hydatid cyst. ($\times 300$.)
Note the pectinate markings on the laminæ.

this layer which causes the incurling of the membrane when the cyst is ruptured. With a couple of pairs of forceps it is possible to strip layer after layer from it, showing that it is composed of a series of laminæ. If a small portion be teased out in glycerin and examined under the microscope, the lamination is easily distinguished; and on further examination under a high power each of these laminæ may be seen to be marked by a series of pectinate stria running at right angles to the plane of the laminæ.

Degenerative changes occur in the hydatid cyst:—

- I. Spontaneous cure, due to absorption or evacuation of the fluid.

This is followed by death of the scolices, fatty degeneration, caseation, and even calcification.

2. Evacuation after suppuration, or after inflammation of the surrounding tissues ; there is then marked softening of the membrane.

NEMATODES, THREAD-WORMS, OR ROUND-WORMS

485. These are for the most part filiform parasites, some of which are found affecting man.

Naked-eye appearances.—They are covered with a thick elastic cuticle, have a mouth, straight alimentary canal, posterior and ventral anus, and are bisexual. The ovary in the female, and the testis in the male, are seen as more or less convoluted tubes according to the species. The genital opening in the female is as a rule near the junction of the anterior third of the body with the posterior two thirds, on the ventral surface. The male cloaca, with or without a spine, is situated near the posterior extremity of the body.

TRICHINELLA SPIRALIS

486. Syn., *Trichina spiralis*.—Perhaps the most important of this order ; it is met with in two positions in man—one, the mature form, in the intestine ; the second, the sexually immature form, encysted in the inter-muscular connective tissue.

The encysted form, the immature trichina, either in the pig or in the human subject, is usually found in the thin muscles of the abdomen, thoracic walls, diaphragm, cervical and laryngeal muscles, front of the thigh, and less frequently in the other parts of the muscular system. To the naked eye the cysts appear as small whitish specks, longer than broad, lying in enormous numbers in streaks or lines in the long axis of the muscular fibres.

Examined under a strong magnifying glass, the small specks are seen to be cysts, in which, coiled up, lie the larval trichinæ. Rupture the cyst with a couple of needles, turn out the trichina, and under the microscope examine the specimen, after staining (§ 102) and mounting (§ 195). It is about $\frac{1}{25}$ of an inch long, and is provided with an alimentary canal and imperfectly developed reproductive organs. Some of the white specks are quite hard and calcareous. If these are treated with hot caustic potash or soda, they remain unaffected, but a

very weak solution of hydrochloric acid dissolves out the hard material and leaves the capsule soft and pliable.

Harden a piece of the trichinous muscle (§ 61 or 63); cut, and with the aid of a lens find a section in which is at least one cyst, stain (§§ 102, 104, or 110 (*b*), and 132), and mount (§ 195 or 199).

($\times 50$).—The cyst is situated between the muscular fibres, which in the immediate neighbourhood are somewhat compressed; it is lemon-

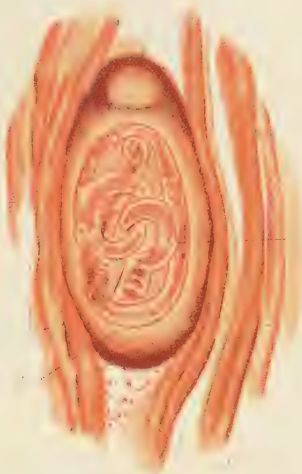


FIG. 262.—*Trichinella spiralis* encysted. Stained with picrocarmine. ($\times 300$.)

- a.* Atrophied muscle fibres.
- b.* Fat cells situated at the end of the cyst.
- c.* Capsule becoming calcified.
- d.* Protoplasm surrounding the worm.
- e.* Trichina coiled up in the cyst.

shaped, and contains the larval worm arranged in one, two, or three coils. At each pole, outside the cyst, a few fat globules, with small blood vessels running amongst them, may be seen. The cyst itself is in the first instance fibrous, being derived from proliferated sarcolemma cells. In the specimen from which Fig. 262 was taken, calcification of this fibrous covering was beginning at the poles. Where complete calcification has taken place, a fibrous covering is still present. Within

the first cyst is a second membranous or chitinous coat which in turn may become calcified, whilst within this again is a quantity of granular protoplasm, in which the worm is imbedded. The complete calcification of the cyst is not completed for about ten months, after which, at an undetermined period, the contained larvæ may undergo fatty degeneration, and even calcification.

($\times 300$).—Corroborate the appearances above described.

Cycle of development of Trichinella spiralis.—When trichinous pork is taken into the alimentary canal, the encysted larval form is set free by the action of the acid gastric juice. On the second or third day it becomes sexually matured. Both sexes are found. The adult male is about $\frac{1}{8}$ of an inch in length, and may be recognised by the two small processes in which the tail ends. The adult female is considerably longer, sometimes twice the length of the male; its body is also thicker, and the posterior extremity is "broad and bluntly rounded." The cloaca in the male is between the lobes of the tail, whilst in the female the genital orifice is placed at about the junction of the anterior third of the body with the posterior two-thirds. On the sixth or seventh day the female gives birth to numerous living sexually immature embryos, which, making their way into the muscular tissue, cause disorganisation of the muscle fibres, and at the end of fourteen days are completely encysted and the cycle is complete; calcification may ensue.

OTHER ANIMAL PARASITES FOUND IN MAN

487. The following further list, selected from Cobbold's "Human Parasites," and Leuckart's "Parasites of Man," may prove of use to the student, who, however, is referred to the original works, and to Manson, Shipley and Sandwith's excellent article on "Parasitic Worms" in Clifford Allbutt's "System of Medicine," 1907, Second Edition, vol. ii. part 2, p. 829 *et seq.*, for fuller descriptions of these parasites.

Trichocephalus trichiurus, syn. *T. dispar*, or whip worm.—A worm about 2 inches long, with a narrow head and neck; the posterior two-thirds, thick like a whip-stock, is curled in the male, but straight in the female; the anterior portion is very thin, like a whip lash. It is very commonly met with embedded in the mucous membrane of the cæcum, and there is usually regarded as harmless, though some cases of appendicitis are said to have been traced to its action.

Filaria bancrofti, syn. *F. sanguinis hominis nocturna*.—The embryo form (*F. sanguinis hominis nocturna*, *Microfilaria nocturna*) is usually found in the blood in the evening, disappearing again in the morning, when it is found in the lungs, heart, and large blood vessels of patients suffering from filariasis: it is about $\frac{1}{30}$ of an inch in length,



FIG. 263.—*Microfilaria nocturna* in blood taken in the evening.
Stained with Giemsa's stain. ($\times 350$.)

pointed at one end, blunt at the other. By its presence in the kidneys it gives rise to chyluria and hematuria. In the fully developed form (*F. bancrofti*) it is a hair-like worm about 3 or 4 inches in length, and is met with in the lymphatics, especially those of the scrotum and lower limbs, giving rise to a condition similar to, if not identical with,

Elephantiasis. It is found especially in China, Australia, and Brazil, the Pacific Islands, and Africa.

Filaria medinensis, syn. *Dracunculus medinensis*—the Guinea worm.—The female,—from the pathological point of view the more important of the sexes,—cylindrical in shape, measuring from 1 to 6 feet in length, and about one-tenth of an inch in diameter, is found in the



FIG. 264.—Drawing of ova of nematode parasites. ($\times 400$.)

a, b, c, and f, by R. Muir ; d, e, after Looss.

- a. Of *Trichocephalus trichiurus*,
- b. Of *Ankylostoma duodenale*, segmented,
- c. Do. containing young embryo,
- d. Of *Oxyuris vermicularis*,
- e. Of *Strongyloides stercoralis*,
- f. Of *Ascaris lumbricoides*—all from fæces, and drawn under the same magnification for purposes of comparison.

subcutaneous tissue of the back or legs, giving rise to swelling and subcutaneous abscess, which bursting, allows the parasite to come to the surface to oviposit in water. It is found especially in India, Arabia, Guinea, the West Indies, Egypt, and Brazil.

Eustrongylus gigas, syn. *Strongylus gigas*, is found in the pelvis of the kidney of dogs and wolves and other fish-eating carnivora ; only a few

cases are recorded in man. The male is about 1 foot long, the female twice that length; the latter is about one-tenth of an inch in thickness; its body is red.

Ankylostoma duodenale, syn. *Dochmius duodenalis*, is found in the duodenum and upper part of the intestine. The male is about three-eighths of an inch long, the female half an inch. It attaches itself by its ventral mouth, which is situated near the anterior extremity, to the mucous membrane, from which it detaches the epithelial covering, and may take blood. Its presence may thus give rise to extensive ulceration and hæmorrhage. It is met with in the West Indies, Cayenne, Brazil, Egypt (giving rise to what is known as tropical anæmia, *Anæmia Egyptica*), and in Northern Italy (St. Gothard Tunnel). It has also been found in America, in Westphalian coal mines, and in Cornish tin mines.

Oxyuris vermicularis, syn. *Ascaris vermicularis*, is the small thread-worm, found in the cæcum and upper part of the colon, especially of children; the male is about one-sixth of an inch in length, the female half an inch.

Strongyloides stercoralis, syn. *Anguillula stercoralis*.—A small nematode at one time associated specially with Cochin-China diarrhœa. It is about $\frac{1}{5}$ of an inch long, and occurs in very great numbers in the whole length of the alimentary canal.

Ascaris lumbricoides, or maw-worm, is a round-worm found in man. It has pointed ends, and is light brown in colour. The male is from 4 to 6 inches long, and has a curved "tail," on which are two sharp spines; the female measures from 10 to 14 inches in length, has a straight tail, and no spines. This worm is found in the upper part of the intestine, but may be present in any part of the alimentary canal, in the bile ducts, and in the peritoneal cavity; it may be ejected with the fæces, or, more rarely, by the mouth.

Ascaris canis, syn. *A. mystax* or *A. alata*.—A small nematode, one-third of an inch in length, found in the alimentary canal of man, and of the cat, dog, and other carnivora.

ARACHNIDA

488. *Sarcoptes scabiei*, or human itch mite, is found in burrows or tunnels in the deeper layers of the skin. The female burrows in the skin, laying her eggs as she goes, and leaving a white track behind her.

Irritation is thus set up, and eczematous or vesicular eruptions result. To obtain the acarus for examination the white line should be found, then the point of entrance to the tunnel, which is marked by a black speck; at the opposite end of the white line the female is found. Cut down on this point with a sharp knife, place the parasite on a slide in a drop of Farrant's solution or glycerin, and examine ($\times 20$). The female mite is about "the size of a small pin-head, and somewhat turtle-shaped." On the under surface are four pairs of legs. The two anterior pairs end in stalked discs, but both the hinder pairs of legs end in setæ. The male is about half the size of the female, and the posterior of his two hinder pairs of legs end in stalked discs; the anterior of the hinder pairs end in long setæ.

Linguatula rhinaria, syn. *Pentastoma tenoides*, of the nasal fossæ of the dog, is the matured form of *Porocephalus* (*Pentastoma*) *denticulatus* of the human liver, spleen, and kidney.

Porocephalus constrictus.—A larger pentastoma, which infests the liver and lungs of man.

Demodex folliculorum, or face mite.—One of the mites met with in the sebaceous follicles of the skin.

Larval form of a *Trombidium* mite, the common species being *T. nolosericeum*. These larvæ were once thought to be a separate species—*Leptus autumnalis*, or harvest bug—a small red mite which infests the skin, giving rise to very irritable papules.

INSECTA

489. *Pediculus capitis*, or head louse.—Found in the scalp.

P. vestimenti, or body louse, which lays eggs and lives in the clothes.

Phthirus pubis, or crab louse.—Found on all hairy parts of the body, but not on the head.

Anopheles maculipennis, or dapple-wing mosquito, the host of the malaria parasite.

Stegomyia fasciata, a mosquito which carries the infective agent of yellow fever.

Glossina morsitans.—Tsetse fly of Africa, described by Dr. Livingstone. The host of the Nagana parasite of animals.

G. palpalis.—The host of the sleeping sickness parasite of the human subject (§ 494).

Stomoxys calcitrans, a greedy, blood-sucking fly, in outward appearance very similar to the common house fly but with a hard pointed—instead of a softer bulb ended—proboscis.

Cimex or *Acanthia lectularia*, or bed bug. — One of the “free parasites.”

Pulex penetrans.—The jigger or chigoe of the West Indies. The female is found in the soles of the feet, beneath the skin.

P. irritans.—The common flea. Another of the “free parasites.”

CHAPTER XVI

MICROSCOPIC PARASITES

A. ORGANISMS FOUND IN PATIENTS SUFFERING FROM MALARIA, KÁLA-ÁZAR, SYPHILIS, AND SLEEPING SICKNESS

490. *Tertian Fever*.—Parasite of mild tertian fever (*Hæmaphysa vivax*) can be found only on most careful examination in unstained blood, as its refractive index is not high.

On to a clean cover-glass (§ 152) take a small drop of blood from near the root of the nail or from the lobe of the ear; invert the cover-glass on to a clean slide so as to obtain a thin equal layer of the fluid blood; ring the cover-glass with vaseline or wax (from a taper) so as to prevent evaporation. Examine under a high power ($\times 800$ or $\times 1000$) in a warm room or on a warm stage, cut down the light from the margin of the field, and when an Abbe illuminator is used, employ a very small aperture of the diaphragm.

It is usually seen as a simple ring-shaped organism; when within the blood corpuscle it may appear to be slightly motile. In larger organisms fine granules of pigment of a yellowish-brown tint are more prominent. These granular masses of protoplasm may be of large size, each with pigment scattered throughout its substance. It then almost fills the red blood corpuscle, which is often increased in size and is dropsical-looking. Here and there the pigment is accumulated into dense, almost black, points. This large protoplasmic mass may be irregular in outline or it may be more definitely rounded or oval; in the latter case the pigment is often concentrated near the centre of the mass. Again we may see a series of more refractile bodies arranged in a kind of rosette occupying almost the whole of the red corpuscle (sporocyte form). These small refractive bodies or spores escape into the blood plasma, whence they again attack the red blood corpuscles and again soon become ring-shaped.

The best period at which to take the blood in order to see the stage of sporulation is during the early stage of the pyrexial period.

Make dry film preparations (§ 59, 152, or 171), stain (§§ 153-157).

($\times 1000$).—Note the young ring-shaped amoebula, with a small mass of deeply stained chromatin, usually in the thinner part of the ring; in the protoplasm are a few granules of pigment. Within the ring

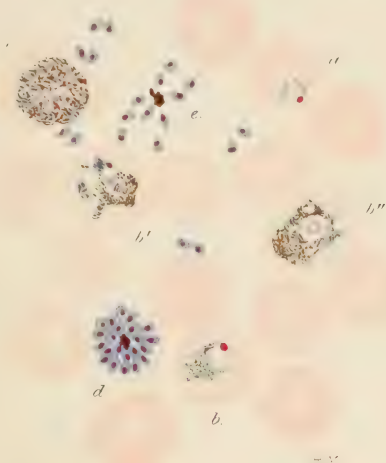


FIG. 265.—Blood film from a case of "simple tertian" malaria.
Stained by Leishman's method. ($\times 1000$.)

- a.* Ring parasite.
- b, b', b''.* Larger ring with granules of pigment.
- c.* Stage of commencing spore formation; pigment being collected into a kind of network.
- d.* Rosette-shaped sporocyte stage.
- e.* Spores lying free in the blood plasma.

a portion of the red blood corpuscle may be seen to be included. In another cell the blue protoplasm is greatly increased in amount, and at one side of the ring the pigment is well developed. In another, the chromatin in the protoplasm is broken up, but is still collected into one area apparently within, or at one side of, the central vacuole. The pigment is also increased in amount, but is still distributed throughout the protoplasm. In still another corpuscle the mass of the protoplasm

is very much enlarged, and occupies a large portion of the red corpuscle; it is, however, breaking up into small rounded blue masses, the red chromatic substance being distributed throughout in fine granules, and in this case apparently occupying somewhat the same position as the brownish granules of pigment. Lastly, this blue protoplasm is seen to be broken up into distinct masses; in the centre of each of these a small chromatic body is placed, a clear space or court being seen on one side of, or around each of the small chromatin masses. Each of these blue, slightly pointed, or irregular ovoid masses, of which there are about twenty in the specimen under observation, is a spore. These spores are arranged around a central mass of brown pigment. We have thus the characteristic "rosette" appearance above described.

This whole group, with the surrounding capsule occupying the greater part of the red corpuscle, constitutes what is called the "sporocyte." Finally, the sporocyte ruptures and sets free the spores, along with the small central mass of pigment, into the blood plasma. The small spores are then spoken of as enhæmo-spores or merozoites. They are usually about $0.75\ \mu$ in one diameter to $1.25\ \mu$ in the other. These organisms go through their various phases of development in forty-eight hours. These phases may be followed in a drop of blood taken from the finger. The enhæmo-spores are afterwards taken into fresh blood corpuscles, and so the process continues. The pigment may be taken up by the mononuclear hyaline cells of the blood, and may be carried to the various parts of the body, where it is often found in the endothelial cells and even in the cells of the perivascular lymphocytes.

491. Blood taken from a case of malignant *Æstivo-Autumnal Fever* does not show parasites in the same stages of development as are seen in the parasite of the mild tertian fever. The ring forms soon develop from the simpler forms, which are highly refractive and can often be seen adhering to the surface of the red blood corpuscles. From the surface they make their way into the substance of the protoplasm of the corpuscle. They remain much smaller than the form above described, but display more active movements. We have in the ring form, which may develop before the corpuscle is invaded, the same zone of blue protoplasm with a small dot of chromatin at one margin, but a comparatively small amount of brown pigment. As these amœbulæ become ring-shaped they gradually lose their amœboid movements. The sporocyte (not seen

in the figure) occupying a shrivelled corpuscle gives rise to a much smaller number of spores, usually from 6-12 merozoites, which have not the definite "rosette" arrangement, and are of small size. These are seldom, if ever, found in the peripheral blood, but may be observed in specimens taken from the spleen. For further descriptions of these parasites, of the pathological conditions associated with them,

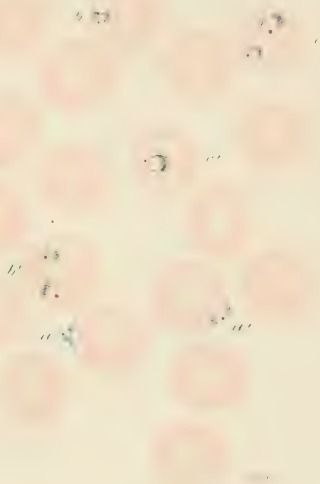


FIG. 266.—Blood film from a case of malignant malaria. Ring forms entering the red blood corpuscles. Stained by Leishman's method. ($\times 1000$.)

- a.a'*. Simple amœbulæ adhering to surface of red blood corpuscles before they penetrate them.
- b.b'*. The simple forms developing into the ring forms.
- c.c'*. Larger ring forms.

for nomenclature, and of cycle of development in the human subject and in the mosquito, *Anopheles maculipennis*, see Muir and Ritchie's "Bacteriology" (§ 206) or special monographs on the subject.

492. *Donovan-Leishman Bodies and Kāla-āzar, Dum-dum fever.*
—Non-malarial remittent fever (China, India), Dum-dum fever, or

Kála-azar (Assam), is a very chronic, but ultimately fatal, form of febrile anæmia. During life it is characterised by marked bloodlessness, accompanied by a very definite fall in the number of leucocytes, greater in proportion than the fall in the red-blood corpuscles, which, however, is considerable. Ulcerations of the cutaneous and mucous surfaces are fairly common, and dropsy is often present, along with enlargement of the liver and spleen. Leonard Rogers notes that these latter, along with ulceration of the lower part of the small intestine and the colon and proliferation of the cells of the bone marrow, are the principal pathological lesions met with at the post-mortem examination.

Make a section of the swollen spleen, and from the freshly cut surface make films on a slide or cover-glass (§ 152), and stain (§ 153).

($\times 1000$).—Lying free or grouped in the large endothelial cells of the spleen are deeply stained points, round, oval or “cockle-shaped”

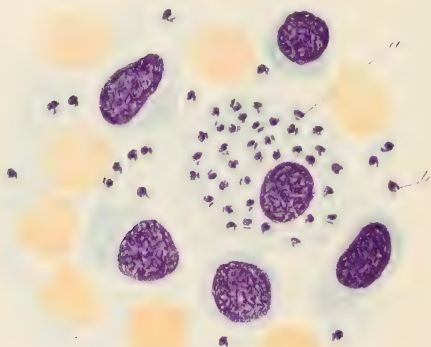


FIG. 267.—Kála-azar. Scraping from spleen. Donovan-Leishman bodies. Stained by Leishman's method. ($\times 1000$.)

- a.* Large endothelial cell of splenic pulp containing numerous Donovan-Leishman bodies.
- b.* Similar bodies lying free between the cells.

bodies, measuring from 3.5 to 2.5μ or even less in diameter. The protoplasm of these bodies—the so-called Donovan-Leishman bodies (after the observers who first described them)—stains somewhat un-

equally of a light blue tint. Embedded in this, usually with a lightly stained area between them, are two very deeply stained corpuscles of unequal size. These take on a violet colour with Leishman's stain, corresponding to that taken on by the nuclei of the surrounding cells. The larger of these corpuscles is not quite so deeply stained as the smaller; it is rounded, oval, conical, or sometimes almost dumb-bell shaped. It is usually seen at one margin of the body, and is said to lie "near the hinge" in the "cockle-shaped" bodies. The smaller and more deeply stained of the corpuscles is thinner and somewhat elongated, and is sometimes described as "rod-shaped"; it may be parallel, at right angles to the larger corpuscle, or running obliquely from it. In some cases these bodies touch, but, as seen in the drawing, they usually appear to be disconnected. Most of the Donovan-Leishman bodies are contained within the protoplasm of the large endothelial or mononuclear splenic cells, or similar cells in the bone-marrow or of certain lymphatic glands. In the capillary vessels and in the lymphatics they appear to have the same relation to the endothelial cells lining these channels and spaces, as they have to the large mononuclear cells in the spleen. It is looked upon by Leishman and Leonard Rogers as constituting an intermediate stage in the development of either a Trypanosome or a Piroplasma.

Examine the organisms in sections of the organs or tissues hardened (§ 58, 63, or 65), stain (§§ 152–157) and dehydrate and mount (§§ 193 and 199).

A somewhat similar organism has been described in the Delhi sore.

493. *Spirochæta pallida* of Schaudinn and Hoffman, or *Spirochaeta pallidum*.—If fluid from a primary syphilitic sore, from any other primary or secondary lesion of a case of syphilis, or from a lymphatic gland nearest to one of these sores, be collected with a hypodermic needle and examined fresh, suspended in a little normal saline solution into which a very few minute particles have been introduced, a number of very delicate spiral-shaped organisms may be seen. Each may consist of half-a-dozen to a dozen well-defined short regular curves which "in plan" appear to be almost semi-circular. These organisms exhibit active screw-like movements as they rotate along their long axes. They may become more or less bow-shaped and then straighten out, and they may alter their position slightly in the field

of the microscope. This organism is not strongly refractile, and cannot be examined except by special central illumination; the movements of the minute particle mentioned above enable this organism to be detected more readily. Dry a film on a cover-glass (§ 59 or 171) or slide (§ 152), and stain (§ 157).

($\times 1000$).—The stained organisms, embedded in the fixed albumin between the lymphocytes and the red cells, stand out as described above as very regular spirals with pointed extremities. They have taken on a delicate reddish tinge which is fairly characteristic of this special spirochæte. The organism usually measures from 4 to 14 μ

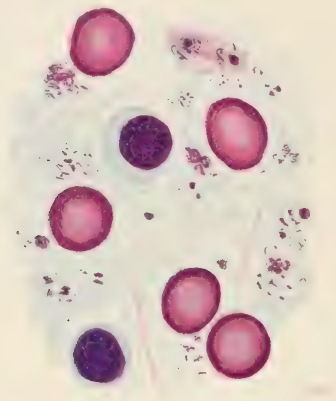


FIG. 268.—Film preparation from primary sore. Syphilis. *Spirochæta pallida*. Giemsa's stain. ($\times 1000$.)

in length: in the specimen figured it measures from 18 to 22 μ in length. It is about 0.25 μ in thickness. In unbroken syphilitic lesions it is unaccompanied by other organisms, but, where these lesions have ulcerated, other organisms may invade the tissues, amongst them, not unfrequently, a much more highly refractile and somewhat larger but more irregular spirochæte, the *Spirochæta refringens*. Here the curves are longer, much less regular, and as they are kept under microscopical examination vary from time to time in length and sharpness. A further distinctive characteristic of this organism is that by Giemsa's stain it is stained of a bluish tint instead of the red tinge assumed by the *Spirochæta pallida*. Flagella

have been demonstrated at the pointed ends of the *Spirochæta pallida*, but no undulating membrane, the syphilitic organism in this differing from the *Spirochæta refringens*. A section of the liver from a case of congenital syphilis may contain an enormous number of these spirochætes. Stain (§ 158). They are seen as dark spirals coated with silver against a pale yellow background. On staining the tissues with weak carbol-fuchsin or toluidin-blue, many of these spirals are seen to be within the liver cell. Similar spirochætes are found in the lung, spleen, and other visceral organs sometimes even in the heart. These organisms have also been found by Schaudinn and Hoffman and Metchnikoff and Roux in lesions produced in the higher apes, especially the chimpanzee, and it is now very generally assumed that they are the primary cause of syphilitic lesions in the human subject. They are certainly present in the lesions usually met with in cases of primary and secondary syphilis of the human subject.

494. *Trypanosoma gambiense*, the trypanosoma of sleeping sickness, is found in the blood, the juice from a lymphatic gland collected by means of the hypodermic needle, or cerebro-spinal fluid of patients suffering from sleeping sickness. Examine at once, unstained.

($\times 300$).—An actively motile, highly refractile organism may be seen, but it is difficult to make out much detail. Under a much higher power ($\times 1000$) it is seen to be a somewhat spindle-shaped organism, one end slightly blunted or rounded, the other prolonged into a pointed flagellum. It moves about rapidly between the red blood corpuscles or other corpuscles or particles, the body having an undulatory movement, and the flagellum moving rapidly, the body following the flagellum. In the body of the protoplasm bright points, more fully described below, may be seen. Stain (§ 157). The spindle-shaped mass of protoplasm, stained blue, is slightly granular. In the centre of the spindle-shaped mass is a very distinct reddish-purple oval body, the nucleus or macro-nucleus, the substance of which, at first sight almost homogeneous, may on careful examination be found to be slightly granular. Near the posterior, or blunt, end is a second but much smaller deeply stained reddish-purple point known as the micro-nucleus or centrosome. These organisms are from 15 to 25 μ in length (without the continuing flagellum, which is from 5 to 6 μ) and from 1.5 to 2.5 μ broad. Around the micro-nucleus the protoplasm is not so deeply stained. Arising from or near this micro-nucleus and

running along the margin of the organism is a narrow band, which has a sharp, very definite, but wavy, free margin. It seems to be continuous with the large spindle-shaped body of the trypanosome, and from the delicate staining when seen "in plan" seems to be thin and to be composed of the same substance as the trypanosome, except at the free margin, where it takes on the red tint of the micro-nucleus. This "undulatory membrane," narrowest at the posterior end, where it commences, gets broader and broader until the micro-nucleus is

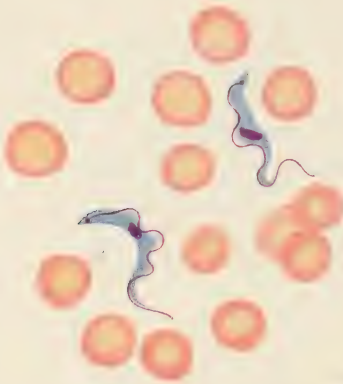


FIG. 269.—Blood film from a case of sleeping sickness. Stained by Leishman's method. ($\times 1000$.)

- a. Blunted end of trypanosome.
- b. Flagellum.
- c. Nucleus or macro-nucleus.
- d. Micro-nucleus or centrosome.
- e. Undulatory membrane, with red "free margin."

reached, and then may taper off irregularly as it passes farther forward until it merges into the flagellum. In sleeping sickness the presence of this organism is usually associated with distinct anæmia, the red cells being diminished in number and the hæmoglobin in quantity. Along with this there is an increased number of mononuclear leucocytes, both large and small, in the blood, and cedema and dropsy are commonly present. The human subject is said to be an intermediary host of this organism, the *Glossina palpalis*, being the primary host, just as *Glossina morsitans* or tsetse fly is the primary host of the trypanosome of

N'gana disease. The trypanosome may be studied in sections of the tissue stained by Levaditi's method (§ 158).

B. SCHIZOMYCETES, FISSION FUNGI, OR BACTERIA

495. In the examination of bacteria it is necessary not only that they should be appropriately stained, but that we should enlist the most accurate microscopic appliances into our service.

These organisms are so minute that it is only by the exercise of the greatest care, and with the aid of the most perfect illuminating apparatus at our command, that many of them are to be recognised, though masses of them may often be readily enough made out lying in blood vessels or lymphatics. When once their presence is determined, their position in the tissues has to be further studied, and this can be done only under the most favourable conditions. In all work of this kind, where possible, use an oil immersion lens and an Abbe's illuminator. This illuminator or condenser has a very short focus, and must therefore be brought up almost to the under surface of the object to be examined. It may also be used as an ordinary condenser, if the lateral or greatly converged rays be cut off by means of a diaphragm with a small aperture, placed below. If a large aperture in the diaphragm be used, the greatly converged rays of light are also allowed to play on the structures, which, lighted from all points, lose all shadows, and the "structural picture" is lost. As the structural picture is lost, however, the specially stained elements, such as the micro-organisms, and the nuclei, are brought out prominently, and can readily be examined. All preparations should be examined with both the small and the large apertures of the diaphragm beneath the condenser. With the smaller aperture the structural elements and the positions of the organisms are observed; as the aperture is increased in size, the organisms become more and more prominent, whilst the structural elements gradually disappear from view.

A specimen of blood taken from the spleen of a mouse, inoculated with anthrax virus, is seen to be charged with jointed, purple, rod-like bodies, which are recognised as anthrax bacilli. Typhoid bacilli are recognised in the same way in a scraping from one of the enlarged soft mesenteric glands from a case of typhoid fever (§ 365). When it is illuminated by means of an Abbe's condenser, and examined ($\times 700$), a number of exceedingly minute, deeply stained, rod-like bodies may

be seen lying between or embedded in the protoplasm of the cells.

A drop of pus from an acute abscess (§§ 229 and 229*a*), similarly treated and examined, presents numerous minute rounded bodies, either in chains or in zoogloea masses, with, here and there, it may be, a few elongated or rod-shaped bodies lying free in the fluid, whilst similar organisms embedded in the pus corpuscles can readily be observed.

A FEW TYPES OF THE SCHIZOMYCETES

Sphaerobacteria (rounded bacteria)

(*a*) *Micrococcus* and (*b*) *Sarcina*

496. Micrococci are the smallest and most elementary vegetable organisms. They are probably divided into cell membrane and cell contents. They may be isolated, or in fours, as in the pyæmia of rabbits; in chains, as in acute suppurative processes, erysipelas, etc.; or in zoogloea masses, united by a glue-like material, as in acute abscesses; in the lymphatics in acute pneumonia, where they are surrounded by a kind of capsule (Friedländer); and in the spreading abscesses of rabbits, as described by Koch.

They appear to increase in number by a process of direct division or fission.

Pathogenetic micrococci, or those which are supposed to be the cause of diseased conditions, are met with in certain of the specific infective diseases.

In *septicæmia* they occur in connective tissue spaces; but also in capillary vessels at the points of junction between the arterial and venous capillaries, where the blood is flowing most sluggishly through the widest area, and where consequently the micrococci are most at rest, as in the glomeruli of the kidney and in the hepatic capillaries of the liver.

In certain forms of *pyæmia*, the micrococci are found in similar masses in the vessels.

In *purulent inflammations* they are usually found either in the connective tissue or on some one or other of the mucous surfaces.

Erysipelas is usually caused by an organism arranged in chains which are found in the lymphatics and connective tissue spaces.

In *endocarditis* (§ 265) streptococci are sometimes present, in other cases staphylococci.

Osteomyelitis (*Staphylococcus pyogenes aureus* or micrococcus of osteomyelitis). (§§ 229, 229a, and 379.)

497. The *Sarcina ventriculi*, described by Goodsir, is frequently met with in the acid watery vomited matter from dyspeptic patients. It occurs in the typical wool-sack formation—the fission taking place

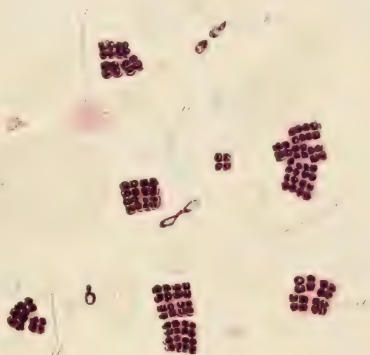


FIG. 270.—Drawing of vomited matter from a dilated stomach. Stained with alum hæmatein and picro-erythrosin. ($\times 1000$.)

- a. *Sarcina ventriculi*.
- b. *Torula*.
- c. Starch granules.
- d. Micrococci.

so as to form masses of fours of small round micrococcioid organisms. A smaller form, *Sarcina pulmonum* (Virchow), is met with in the lungs, pharynx, and urine. It has a green tinge.

Microbacteria (Short Bacteria)

498. These are the short rod- or egg-shaped bodies with rounded extremities, which are found in the hemorrhagic septicæmias, fowl and hog choleras, and similar diseases. The pneumococcus and the

gonococcus, which latter is made up of two apposed discs, with a clear intermediate band, really belong to this group.

Desmobacteria (Ribbon-shaped Bacteria)

499. These are ribbon or thread-shaped organisms, which appear at some stage of their existence to be composed of strings of short rods. The strings may be composed of two or three segments only, or there may be a considerable number in each chain, whilst in some cases again, or at certain periods in their life-history, the long filament is present, but is quite unsegmented. The most important of these are the following.

Bacillus anthracis—the bacillus associated with splenic fever,

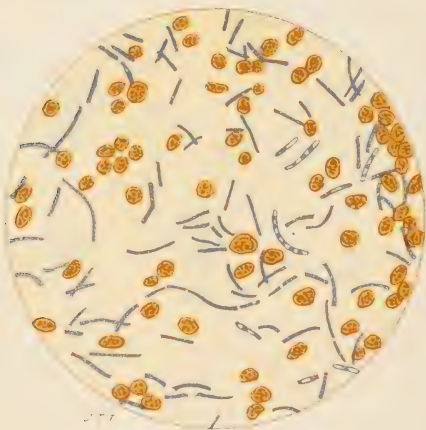


FIG. 271.—*Bacillus anthracis* from the spleen of a cow that succumbed to an attack of splenic fever. The specimen was taken some time after the organ had been removed from the carcase, and, in presence of air, spores had begun to form in the bacilli. The specimen was dried, heated, stained by Gram's method, with methyl-violet and vesuvin, and mounted in Canada balsam. ($\times 700$.)

The anthrax rods and filaments, some of them with bright points, spores, are stained with methyl-violet. The cells of the splenic pulp are stained brown by the vesuvin.

malignant pustule, charbon, and intestinal mycosis—is from 4 to 20 μ in length, and about 1.5 μ in thickness. In the serous fluid thrown

out into the pleura in such cases, the rods are as much as $150\ \mu$ in length (these may have continued growing after the death of the patient).

This organism is found, especially in the capillary vessels, at the points where the blood flow is most retarded. It may be present in such quantities as to cause plugging, distension, and rupture of the vessels, especially of the abdominal and thoracic viscera. Like the other members of the group, it begins as a spore, which goes through certain phases of development before it assumes the form of a rod-shaped bacillus. Under favourable conditions the threads attain to as much as ten or twenty times the original length of the bacillus; the protoplasm of which it is composed becomes granular; highly refractile spores are formed in this at regular intervals: after which the thread breaks up into lengths, the spores are set free, and the same process begins again. In place of this series of changes the bacillus may undergo simple division, especially in the blood of the living animal, as in splenic fever and in septicæmia of the mouse (Koch). The spores are never formed, except in the presence of free oxygen,—in the blood that has escaped from the body, for example.

Bacillus of typhoid fever (§ 365). This occurs in two forms; as short rods with rounded ends, 2 to $4\ \mu$ in length and $0.5\ \mu$ in breadth, and



FIG. 272. Drawing of young agar cultures of (a) *Bacillus typhosus* and (b) *Bacillus coli communis*. Stained with fuchsin. ($\times 1000$.)

Note the greater length (in some cases definite threads are formed) but slightly less diameter of the typhoid bacillus. In both, diplobacilli with rounded ends are seen, the *Bacillus coli communis* being the shorter and plumper of the two.

as long rods, 8 to $10\ \mu$ in length. These latter are especially common in cultivations; both forms may be found in the intestinal ulcers, but usually only the short rods in the spleen, kidney, liver, and blood

(Koch, Eberth, Gaffky). Examine unstained in hanging drop of normal saline solution for motility. Stain (§§ 178–181) and examine for flagella.

Bacillus coli communis is somewhat like the *B. typhosus*, but is usually somewhat shorter and in a hanging drop is said to be less active. Stain and examine as above (*B. typhosus*).

Bacillus tuberculosis, already described (§ 333).

Bacillus lepræ, which is best stained, as for tubercle bacilli (§§ 182, 183, and 333) is a straight or slightly curved rod, 3 to 4 μ in length, 0.3 μ in breadth, often contains spores or is broken up into short coloured sections with clear spaces between, and is embedded in the cells of the nodules found in leprosy (§ 247).

Bacillus mallei or *glanders bacillus* is a small non-motile bacillus usually about 2 to 4 μ in length and 0.5 μ broad, though it may in a few cases attain a length of 8 to 12 μ . It is found within, or more frequently, around the cells of the glanders nodules. Stain (§§ 122 and 188) and decolorise (§ 193) with anilin oil. When inoculated it gives rise to a characteristic attack of glanders.

Bacillus of tetanus.—A rod-shaped organism which in young cultures is distinctly flagellated. Stain (§§ 173–181.) The spore is terminal, and when spore formation begins, the organism assumes a drumstick shape. It is usually about 4 to 5 μ long and 0.4 μ broad, and has rounded ends, though long threads may make their appearance in cultivation.

Spirobacteria (Spiral Bacteria)

500. The *cholera bacillus*, Koch's comma-shaped bacillus, belongs to this group. It is found in the liquid stools during the early stages of the disease. Stain in a watery solution of fuchsin.

It is a curved (comma-shaped) organism, 1.5 to 2 μ in length and 0.4 μ in thickness. Sometimes a couple may be seen forming an "S" or "O." Examined fresh it is seen in swarms moving actively in one direction across the field of the microscope. In cultivations it may grow into long spirals. Stained for flagella (§§ 178–181) a single or double terminal thread may be demonstrated.

In this group was placed at one time another spiral or screw-shaped organism or spirillum, the *Spirochaeta Obermeyer*i, which is found in the blood in cases of relapsing fever. It is now, however, relegated to the group to which the parasites of syphilis belongs. It must be examined in the fresh condition, as it rapidly breaks down, even in such an innocuous fluid as normal saline solution. Examined in the living

blood on a warm stage, it is seen as a very active spiral organism, which is usually two, three, or four times the length of the diameter of a coloured blood corpuscle.

FUNGI, ASPERGILLI, ETC.

501. For the examination of fungi, aspergilli, mucors, saprolegnia, etc., the following method will be found to be particularly convenient. Place the fungus in a watch-glass containing a mixture of two parts of absolute alcohol and one part of liquor ammoniæ. Allow it to remain for two or three minutes, and transfer to a slide on which is a drop of distilled water—or glycerin, if the specimen is to be kept as a permanent preparation—and mount.

The most important of the hyphomycetes or moulds are—

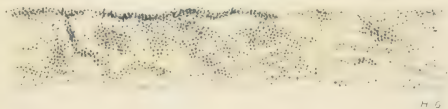


FIG. 273.—Shaft of hair immediately above root bulb taken from a case of ringworm. Stained by Weigert's method. ($\times 90$.)

Note the great number of mycelial threads with numerous large spores surrounding the hair (ectothrix). These may often be seen invading the hair between the margins of the imbricated scales (endothrix).

Achorion schönleinii (favus fungus, forming the yellow cup-shaped masses around hairs), found in the root sheath of the hair bulb, in which the jointed hyphæ or rod-shaped filaments, with clear globules within; rounded spores or groups of spores (conidia) may be found amongst the epithelial cells. It may be prepared by fixing the outer end of the hair to the slide with paraffin, staining in methylanilin-violet, washing carefully in distilled water, and mounting in glycerin. It may also be soaked in water, and treated with caustic potash or acetic acid, and then stained by Gram's or Weigert's method (§ 173), clearing up with anilin oil and xylol, or it may be treated with a mixture of alcohol two parts, ammonia one part, and then mounted in distilled water. Several other fungi have been described as present around the hairs of a favus patch.

Trichophyton tonsurans, *Tinea tonsurans*, or ringworm fungus. Fix the hairs to the slide in the manner directed above, after soaking

them in chloroform; then macerate in 10 per cent. caustic potash for five minutes, wash out the potash with water and examine at once or after staining as above. The fungus is seen in the form of slender jointed rods and small highly refractile spores; these spread not only into the sheath, but also up the shaft of the hair.

Microsporon furfur, *Tinea* or *Pityriasis versicolor* occurs as yellowish or brownish-red patches, covered with thin scales. Scrape off a few of these scales with a knife, treat as above, and examine under the microscope. The microsporon is seen as thin curved filaments, the conidia are grouped into masses, whilst short spore-bearing filaments forming a dense network may also be seen.

Actinomyces (Ray Fungus)

502. Actinomycosis was long mistaken for tuberculosis, and for certain forms of new growth such as osteosarcoma.

The fungus itself appears as (*a*) long branching filaments about 0.5 to 0.6 μ in diameter, forming an open or dense felted network, the strands near the periphery having an irregularly radiating arrangement. These threads are embedded in a homogeneous matrix; they have an endoplasm which may be segmented, surrounded by a sheath. (*b*) Spherical bodies arranged in rows in long tubes which grow from the felted network in cultivation; and (*c*) a rosette-shaped or star-shaped growth, formed of a central body, from which club-shaped masses radiate. As these grow, a proliferative irritation is set up around them, and a structure, similar in most respects to that of tubercle, is formed. In some of these masses, especially those of rapid growth abscesses and fistulae, from which a pus containing the actinomyces, "small white or yellow (or reddish) greasy-looking masses lying among the purulent detritus," is discharged. These may be recognised with the naked eye, but much more readily under the microscope. In cattle the masses do not break down nearly so readily as in man, and sections of the tissues containing the fungus are easily made after hardening in absolute alcohol. Remove all fatty matter with potash or ammonia, and dissolve out any calcareous particles with weak hydrochloric acid. Then stain for half an hour in the following—

Methylene-blue, 1 per cent. in distilled water	35 c.c.
Eosin, 1 per cent. in distilled water	45 "
Distilled water	100 "

Rinse in water, "dehydrate in absolute alcohol, and place in absolute alcohol to which a few drops of a 1 per cent. solution of caustic potash in absolute alcohol have been added," until the section becomes pink. Wash in 1 per cent. acetic acid in water until it turns bright blue.

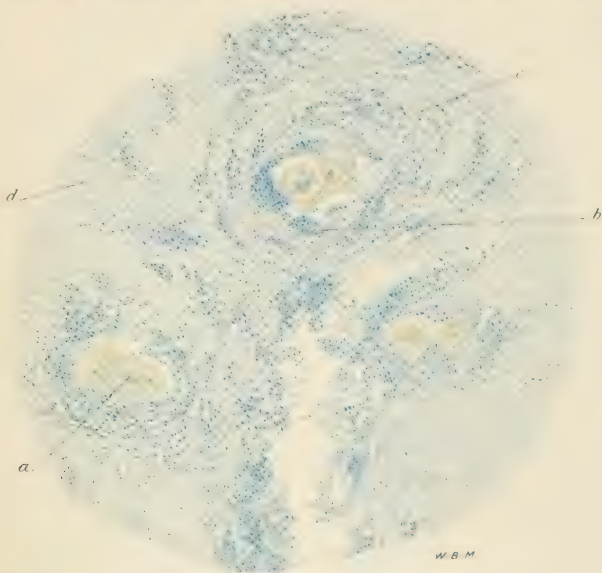


FIG. 274.—Fibrous nodule from a case of actinomycosis (from the tongue of a cow). Stained with Spiller's blue. ($\times 50$.)

- a.* Fungus growing in the centre of a follicle.
- b.* Large endothelioid cells near the fungus.
- c.* Fibro-cellular tissue away from the centre of the follicle, in which round cells predominate.
- d.* More fibrous tissue, still further from the fungus, forming a fibrous capsule.

Dehydrate (§ 193) and mount in xylol balsam (§ 198). The fungus is stained blue, the tissues red (James Miller).

The nodules are usually of considerable size; and when this is the case, they are found to be made of several or numerous follicles, as in tubercle. The tumours may be as large as the fist or even larger.

The granulation tissue, endothelioid cells, fibrous bands, and the rest may all be distinguished ($\times 50$ and $\times 300$) as in tubercle.

In cattle the positions in which the disease most frequently occurs



FIG. 275.—Actinomycosis. Tongue of cow. Section stained in Spiller's blue. ($\times 300$.)

- a.* Centre of mass of conidia (conidiophore).
- b.* Pear-shaped conidia.
- c.* Endothelioid cells. (Compare these with the cells seen near the centre of a tubercle follicle (Fig. 58).)
- d.* Fibrillar tissue near the margin of the follicle.
- e.* Spindle-shaped cells, seen especially near the margin.

are the lower and upper jaws, and first part of the alimentary canal; in the human subject the soft parts of the neck, the mediastinal tissue, the lungs, and the vermiform appendix are specially affected (see also § 251 (4)).

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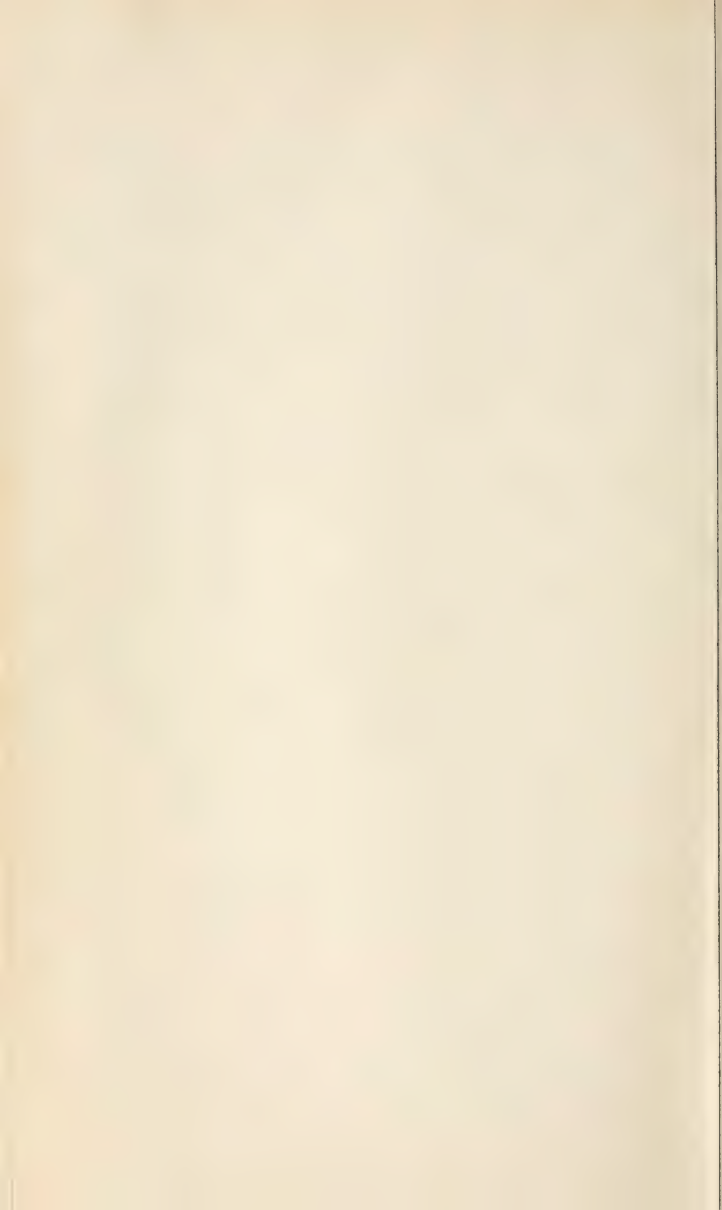
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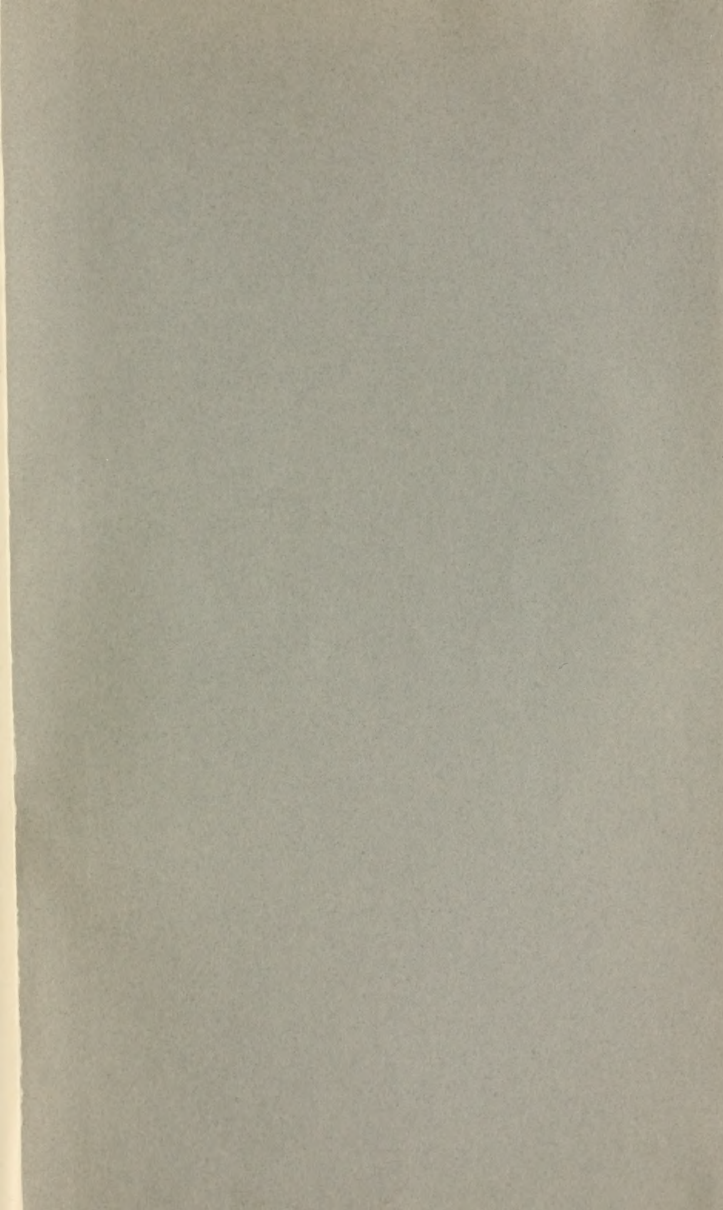
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